# (19) World Intellectual Property Organization International Bureau





# (43) International Publication Date 24 January 2002 (24.01.2002)

## **PCT**

# (10) International Publication Number WO 02/06513 A2

(51) International Patent Classification<sup>7</sup>: C12Q 1/00

(21) International Application Number: PCT/US01/16525

(22) International Filing Date: 13 July 2001 (13.07.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/218,118 13 July 2000 (13.07.2000) US 60/283,880 13 April 2001 (13.04.2001) US

(71) Applicant (for all designated States except US): PHAR-MACIA & UPJOHN COMPANY [US/US]; 301 Henrietta Street, Kalamazoo, MI 49001 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): HOMA, Fred, L. [US/US]; 3430 Pine Grove Lane, Kalamazoo, MI 49008 (US). WATHEN, Michael, W. [US/US]; 6474 Pepperidge, Portage, MI 49002 (US). HOPKINS, Todd, A. [US/US]; 744 Sarah Street, Galesburg, MI 49053 (US). THOMSEN, Darrel, R. [US/US]; 6916 Willson Drive, Kalamazoo, MI 49009 (US).

(74) Agent: YANG, Lucy, X.; Intellectual Property Legal Services, Pharmacia & Upjohn Company, 301 Henrietta Street, Kalamazoo, MI 49001 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published:

 without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



1/06513 A2

(54) Title: A METHOD FOR TREATING HERPES VIRUSES

(57) Abstract: The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvrus in a human host in need of such treatment. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpsvrus in a human host in need of such treatment.

## A METHOD FOR TREATING HERPES VIRUSES

#### FIELD OF THE INVENTION

The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpes viruses in a human host in need of such treatment.

5

10

15

25

30

#### BACKGROUND OF THE INVENTION

The herpesviruses comprise a large family of double stranded DNA viruses. Eight of the herpes viruses, herpes simplex virus types 1 and 2 (HSV-1 and HSV-2), varicella zoster virus (VZV), human cytomegalovirus (HCMV), Epstein-Barr virus (EBV), and human herpes viruses 6, 7, and 8 (HHV-6, HHV-7, and HHV-8), have been shown to infect humans. Several of these viruses are important human pathogens.

HSV-1 is estimated to affect 100 million people in the U.S. Primary infection of HSV-1 usually occurs between the ages of one and four. Cold sores, the visible symptom, typically appear at a later age, with 20-45% of the population over the age of fifteen affected (Whitley, Clin. Intect. Dis., 26:541-555, 1998).

Genital herpes (HSV-2) is the second most common sexually transmitted disease, with approximately 22% of the U.S population infected with this virus (Fleming 1997).

VZV is the causative agent of chicken pox upon primary infection and can recur in adults as zoster.

EBV results in approximately two million cases of infectious mononucleosis in the U.S. each year. It can also cause lymphomas in immunocompromised patients and has been associated with Burkitt's lymphoma, nasopharyngeal carcinoma, and Hodgkins disease.

Infection with HCMV often occurs during childhood and is typically asymptomatic except in immunocompriomised patients where it causes significant morbidity and mortality.

HHV-6 is the causitive agent of roseola and may be associated with multiple sclerosis and chronic fatigue syndrome. HHV-7 disease association is unclear, but it may be involved in some cases of roseola. HHV-8 has been associated with Karposi's sarcoma, body cavity based lymphomas, and multiple myeloma.

These viruses are capable of residing in a latent state within the host. Reactivation of latent virus results from response to environmental stimuli (ex. UV exposure, stress,

etc.). Infections or recurrence can be life threatening in immunocompromised patients such as AIDS or transplant patients where HCMV can result in retinitis, pneumonia, and gastrointestinal disease.

The increased immunocompromised population has created an unmet medical need for antivirals against herpesviruses because current therapies do not have a sufficiently broad spectrum against this family of viruses and/or they have limited utility due to toxicity. The present invention provides a method for selectively inhibiting herpesviruses DNA polymerase with compounds that have broad spectrum activity. The method offers a distinct advantage in the treatment of patients in need, particularly immunocompromised patients at risk of infection or reactivation by many members of the herpesvirus family.

## SUMMARY OF THE INVENTION

The present invention provides a method of selecting compounds that inhibit herpes viruses comprising:

- 15 a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type herpes virus,
  - b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant herpes virus which is the same strain of the wild type herpes virus,
  - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and

5

10

- d) selecting the compound of interest wherein the IC<sub>50</sub> of step b is at least 3 times 20 greater than the IC<sub>50</sub> of step a.
  - In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type HSV-1,
- 25 b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain of the wild type herpes virus,
  - c) comparing  $IC_{50}$  of step a with  $IC_{50}$  of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.
- In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type HSV-2,

b) measuring  $IC_{50}$  of the same compound that inhibits a binding domain mutant HSV-2 which is the same strain of the wild type herpes virus,

c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and

5

15

20

25

30

d) selecting the compound of interest wherein the IC<sub>50</sub> of step b is at least 3 times greater than the IC<sub>50</sub> of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type HCMV,
- 10 b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant HCMV which is the same strain of the wild type herpes virus,
  - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.

In above method, the order of step a and step b are interchangeable.

The present invention further provides a method for selectively treating diseases caused by herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein said compound inhibits herpes viruses by interaction with the binding domain in the viral DNA polymerase.

The present invention further provides method for selectively inhibiting herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein  $IC_{50}$  of the compound that inhibits a binding domain mutant herpes virus is at lease 3 times greater than  $IC_{50}$  of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

The present invention further provides a compound for treating herpesviral infections in a human host wherein  $IC_{50}$  of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than  $IC_{50}$  of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

The present invention further provides a compound for treating herpesviral infections in a human host wherein said compound inhibits the herpesvirus by interacting with the binding domain in the viral DNA polymerase.

The present invention further provides a compound for the inhibiting of herpesvirus DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said

compound results in a change of the wild type HSV-1 polymerase at amino acid 823 from valine to alanine.

The present invention further provides a compound for inhibiting herpesvirus DNA polymerases wherein serial passage of a wild type herpes virus in the presence of said compound results a change of the wild type HCMV polymerase at amino acid 823 from valine to alanine and at amino acid 824 from valine to leucine.

5

10

15

20

25

30

The present invention further provides a mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.

The present invention further provides a mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEO.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

# BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 – examples of 4-oxo-DHQ and 4-oxo-DHTP compounds.

Figure 2 – Herpesvirus' polymerases amino acid conserved region.

Figure 3 – Recovered virus after serial passage of HSV-1 in presence of 20  $\mu M$  of compound No. 17.

Figure 4 – Comparision of Wild HSV-1 and HSV-2 herpesvirus DNA polymerase amino acid sequences alligned by amino acid homology. (Seq. No: 14-19)

Figure 5 – Mutant Herpes Virus DNA and amino acid sequence list. (Seq. No: 1-12)

Figure 6 – Wild HCMV herpesvirus DNA polymerases amino acid sequence. (Seq. No 13)

# DETAILED DESCRIPTION OF THE INVENTION

A key enzyme in the replication of all herpesviruses is the virus-coded DNA polymerase. Most of the currently available anti-herpes drugs target the viral DNA polymerase. Drugs such as Foscarnet acts by direct inhibition of the viral polymerase. These drugs are non-nucleoside inhibitors of herpesvirus DNA polymerases. Others such as the nucleoside analogs, Acyclovir, Penciclovir and Ganciclovir must first be phosphorylated to the monophosphate forms by virus encoded kinases and, further phosphorylated to triphosphate by cellular enzymes before they are active inhibitors. The triphosphate forms of these nucleoside analogs inhibit polymerases by competing with the binding of natural

5

10

15

20

25

triphosphates and their subsequent insertion into growing DNA strands. These drugs are known as nucleoside inhibitors of herpesvirus DNA polymerases.

One of the limitations of the currently available drugs is that they are active against only a few of the eight human herpesviruses. For example, Acyclovir and Penciclovir inhibit HSV and VZV replication but have poor activity against CMV.

In order to identify antiviral compounds that would have the potential to inhibit replication of most of the human herpesviruses, compounds are *in vitro* screened for inhibitors of herpesvirus DNA polymerase activity. Because portions of the amino acid sequence of the polymerases are highly conserved within the herpesvirus family it is possible to discover small molecules that inhibit herpesvirus polymerases but not cellular DNA polymerases. Using this biochemical approach, several new classes of compounds such as the 4-hydroxyquinoline derivatives (4-HQ), 4-oxo-dihydroquinoline derivatives (4-oxo-DHQ) and 4-oxo-dihydrothienopyridine derivatives (4-oxo-DHTP) were discovered as potent, non-nucleoside herpesvirus DNA polymerase inhibitors. *In vitro* polymerase assays and/or *in vivo* cell culture assays have demonstrated that these compounds inhibit HSV-1, HSV-2, HCMV, VZV, EBV, and HHV-8 replication.

4-Oxo-DHQ and 4-oxo-DHTP are derivatives of formula I

Ι

wherein ring A is a saturated or unsaturated fused double or triple heterocyclic ring having 1, 2, 3 or 4 heteroatoms selected from group consisting of oxygen, sulfur, or nitrogen; and wherein R and X are the appropriated substitutents, respectively.

Examples of 4-HQ compounds, 4-oxo-DHQ compounds and 4-oxo-DHTP compounds are illustrated in **Figure 1**.

Antiviral activity of these examples are shown in Table 1 below. As shown in Table 1, these compounds inhibit HSV-1 and HSV-2 as well or better than the current commercially available drug Acyclovir.

Table 1
Antiviral Activity of 4-oxo DHQ/4-oxo DTHP Against HSV-1 and HSV-2

	Compound IC <sub>50</sub> (uM)								
virus	1	2	3	4	5	ACV			
HSV-1 KOS	2.0	3.8	3.2	3.2	3.3	3.6			
HSV-1 F	2.5	2.3	2.2	2.1	2.6	1.3			
HSV-1 DJL	2.5	2.6	1.8	2.2	2.7	1.8			
HSV-1 Patton	ND	5.3	7.7	4.3	10	9.3			
HSV-2 MS	2.0	2.5	2.8	2.5	2.5	10			
HSV-2 35D	ND	5.4	5.0	3.2	8.1	6.0			
HSV-2 186	2.0	2.3	3.2	2.3	4.2	>10			

It has also been discovered that point mutations within the HSV-1 polymerase gene that confer resistance to Acyclovir and other nucleoside analogs do not result in resistance to the 4-HQ, 4-oxo-DHQs or 4-oxo-DHTPs. Serial passage of wild type HSV-1 in the presence of 4-oxo-DHQ results in the isolation of mutants that are highly resistant (>20 fold increase in the IC<sub>50</sub>) to these compounds while retaining sensitivity to nucleoside inhibitors such as Acyclovir.

5

10

15

20

25

In order to determine the mechanism of action of 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds against herpes viruses, mutants resistant to these compounds are isolated by serial passage of the virus in the presence of a 4-oxo-DHQ compound. Sequencing analysis of HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ identifies that HSV-1 (KOS strain) polymerase protein and its homologous HSV-2 have a conserved region (a binding domain), which is a critical contact point for these compounds. While amino acid numbering of the DNA polymerase may vary between strains of HSV-1 and HSV-2, this binding domain encompassing the HSV-1 (KOS) strain amino acid 823 is highly conserved in herpesviruses and can be identified by alligning the homologous amino acids of this domain as shown in Fig 2.

In HSV-1 and HSV-2 strains resistant to the 4-oxo-DHQ and similar compounds, a change of valine to an alanine at the binding domain provides full resistance.

In the HSV-1 DNA polymerase, resistance is also found when a valine changes to methionine at amino acid 823 but only when accompanied by a second amino acid change.

Isolation of HCMV resistant to 4-oxo-DHQ's is found to be very difficult. Comparison of the amino acid sequence of the HSV polymerase (Y-G-F-T-G-V-Q-H-G) and HCMV polymerase (Y-G-F-T-G-V-V-N-G) in the region of amino acid 823 (underlined amino acid) shows that there is a second valine at position 824 in the HCMV

polymerase. In vitro assay using mutant HCMV polymerases demonstrates that full resistance to the 4-oxo-DHQs requires changes at both amino acids 823 (a valine to alanine) and 824 (a valine to leucine). A HCMV polymerase gene containing V823A and V824L mutations is used in marker rescue experiments to generate a viral mutant. This mutant has an IC<sub>50</sub> approximately 7-fold above that of wild-type HCMV.

The HSV-1, HSV-2 and HCMV mutants are also found to be resistant to other non-nucleoside inhibitors such as the 4-oxo-DHTP and similar compounds. However, when the binding domain mutants (e. g. HSV-1 V823A, HSV-2-MS V826A, HSV-2-186 V828A, and HCMV V823A/V824L mutants) are tested in plaque reduction assays against a series of nucleoside polymerase inhibitors and the non-nucleoside inhibitor such as Foscarnet, replication of the mutants is found to be inhibited by all of the currently marketed anti-herpes polymerase inhibitors tested.

These studies demonstrate that certain non-nucleosides like 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds bind to a different site on the herpes polymerase than the nucleoside inhibitors and Foscarnet. The valine at the binding domain is conserved in the DNA polymerases of six of the eight human herpesviruses and several animal herpesviruses, and appears to play a critical role in the antiviral activity of the 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP compounds. (See **Figure 2**)

Since mutation at the binding domain negates these non-nucleoside inhibitors' activities, compounds could be tested against wild type polymerases and the mutant polymerases to establish the probability of similar binding. We refer to this property of compounds as interaction with the binding domain. Since compounds that interact with the binding domain have exhibited broad-spectrum activity against herpesviruses, this invention provides a method for selecting compounds to treat individuals such as immunocompromised patients who are afflicted with multple herpesvirus infections.

# **Definitions**

5

10

15

20

25

30

The term "wild-type" refers to a gene or gene product which has the characteristics of that gene or gene product when isolated from a naturally occurring source. A wild-type gene is that which is most frequently observed in a population and is thus arbitrarily designated the "normal" or "wild-type" form of the gene.

In contrast, the term "mutant" refers to a gene or gene product which displays modifications in sequence and or functional properties (i.e., altered characteristics) when

compared to the wild-type gene or gene product. It is noted that naturally-occurring mutants can be isolated; these are identified by the fact that they have altered characteristics when compared to the wild-type gene or gene product.

IC<sub>50</sub> refers to concentration of a drug that inhibits virus growth by 50%.

Wild type HSV-1 and HSV-2 strains are listed in Figure 4.

Wild type HCMV is listed in SEQ. ID. NO.13.

5

10

15

20

25

30

The term "Iudr" refers to antiviral drug Iododeoxyuridine.

The term "Bvdu" refers to antiviral drug Bromovinyldeoxyuridine.

The term "ACV" refers to antiviral drug Acyclovir.

The term "AraC" refers to antiviral drug Arabinosylcytidine.

The term "AraT" refers to antiviral drug Arabinosylthymine.

The term "AraA" refers to antiviral drug Arabinosyladenine.

The term "GCV" refers to antiviral drug Ganciclovir.

The term "CDV" refers to antiviral drug Cidofovir.

The term "PFA" refers to antiviral drug Foscarnet.

The term "binding domain" refers to a conserved region in herpesvirus DNA polymerases. The herpesvirus DNA polymerases have seven (7) conserved regions. The binding domain is within the thrid conserved region (see Figure 2). When the binding domain contacts with an inhibitor, at least one amino acid in the binding domain mutates and provides the resistance. In general, the binding domain is at an amino acid sequence position 818-829 of the HSV-1 DNA polymerase or the homologous region in other herpes virus DNA polymerases (see Figure 2).

The term "a binding domain mutant herpes virus" refers to a herpes virus containing a binding domain mutation.

More specifically, the binding domain in HSV-1 strains, KOS, F, DJL and Patton are at amino acid sequence position 823. The binding domain in HSV-2 MS-M1 strain is at amino acid sequence position 826. The binding domain in HSV-2 186 strain is at amino acid sequence position 828. The binding domain in HCMV AD 169 strains is at amino acid sequence position 823-824.

The term "XxxxY" refers to an amino acid sequence position xxx, a single amino acid X in wild type is changed to an amino acid Y.

For example, the term "V823A" refers to an amino acid sequence position 823, a Valine found in wild type is changed to alanine in mutant strain.

The term "V824L" refers to an amino acid sequence position 824, a Valine found in wild type is changed to Leucine in mutant strain.

The term "V826A" refers to an amino acid sequence position 826, a Valine found in wild type is change to alanine in mutant strain.

The term "V828A" refers to an amino acid sequence position 828, a Valine found in wild type is change to alanine in mutant strain.

A table of amino acids and their representative abbreviations, symbols and codons is set forth below in the following Table.

U

15

20

5

Amino acid	Abbrev.	Symbol			Co	don(s)		
Alanine	Ala	Α	GCA	GCC	GCG	GCU		
Cysteine	Cys	С	UGC	UGU				
Aspartic acid	Asp	D	GAC	GAU				
Glutamic acid	Glu	Е	GAA	GAG				
Phenylalanine	Phe	F	UUC	UUU			<u> </u>	
Glycine	Gly	G	GGA	GGC	GGG	GGU		
Histidine	His	H	CAC	CAU				
Isoleucine	Ile	I	AUA	AUC	AUU			
Lysine	Lys	K	AAA	AAG				
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU
Methionine	Met	M	AUG					
Asparagine	Asn	N	AAC	AAU				
Proline	Pro	P	CCA	CCC	CCG	CCU		
Glutamine	Gln	Q	CAA	CAG				
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU
Threonine	Thr	T	ACA	ACC	ACG	ACU		
Valine	Val	V	GUA	GUC	GUG	GUU		
Tryptophan	Trp	W	UGG					
Tyrosine	Tyr	Y	UAC	UAU				

## MATERIALS AND METHODS

# Cell and Viruses

African green monkey kidney cells (Vero) and human foreskin fibroblast cells (HFF) and herpes viruses can be obtained from the American Type Culture Collection (ATCC). Media is defined as Dulbecco's modified Eagle media (DMEM) containing 10% fetal bovine serum (FBS) and supplemented with antibiotics. Cells are maintained in media at 37°C in a humidified atmosphere of 5% CO<sup>2</sup>. HSV-1 strains F, Patton and DJL, HSV-2 strains MS, 35D and 186, and HCMV strain AD169 are used in these studies. Strain DJL is a clinical isolate of HSV-1 isolated in our lab from a primary oral lesion.

# Measuring IC<sub>50</sub> of a Compound of Interest That Inhibits Herpes Viruses

5

10

15

20

25

30

Preparation of Virus Stocks: HSV-1 and HSV-2 stocks are grown in Vero cells. HCMV stocks are grown in HFF cells. Approximately 1 ml of media containing sufficient virus to infect approximately 0.1% to 1% of the cells (multiplicity of infection of 0.001 to 0.01 PFU/cell) is added to a T-150 cell culture flask containing a confluent monolayer of cells. The cells are incubated at 37°C for approximately 1 hour. Approximately 50 ml of media is then added to the flask and the cells are incubated at 37°C until viral cytopathic effect (cpe) is apparent in 100% of the cells. The flask is then placed at –80°C for at least 30 min. The flask containing frozen media and cells is placed in a 37°C water bath until the media is thawed. This process disrupts the cells and releases virus into the media. 1 ml aliquots of media containing virus are dispensed into tubes and stored at –80°C. These aliquots of media containing virus are referred to as virus stocks.

Titrating Virus Stocks: Aliquots of virus are thawed at 37°C and serially diluted (10 fold dilutions) in media. 0.1 ml of each dilution of virus is placed in a single well of 24-well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV) and incubated at 37°C for 1 h. The virus innoculum is then removed and 1 ml of media containing 0.8% carboxymethylcellulose (CMC) is added to each well of the dish. The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. The virus titer which is expressed as plaque forming units (PFU) per ml is obtained by counting the plaques in a well and correcting for the dilution of the viral innoculum.

Plaque Reduction Assays: Antiviral activity of compounds against herpesviruses such as HSV-1, HSV-2, or HCMV can be measured using plaque reduction assays. 0.1 ml of media containing approximately 50 PFU of virus is added to each well of a 24-well cell culture dish containing a confluent monolayer of cells (Vero cells for HSV-1 and HSV-2, HFF cells for HCMV). Compounds are dissolved in 100% DMSO and diluted in 100% DMSO as 200x stocks of the desired final drug concentration. Typically 5-6 two-fold dilutions are prepared for each compound. Dilutions of compounds are then added to media containing 0.8% CMC resulting in a final 1x drug concentration. After the virus-infected cells have incubated for 1 h at 37°C, the virus innoculum is removed and 1 ml of media containing 0.8% CMC and the various concentrations of compound is added to each well of the dish.

The dish is incubated at 37°C for approximately 2-3 days (HSV-1 and HSV-2) or 6-9 days (HCMV) to allow sufficient growth of virus to form plaques in the cell monolayer. Plaques can be observed and counted microscopically or by staining the cells with 0.1% crystal violet in 20% ethanol. Virus inhibition is determined for each drug concentration by comparing the number of plaques in drug-containing wells to control wells that did not contain drug. Antiviral activity of a compound is expressed as the concentration of compound predicted to reduce the number of plaques in a well by 50% (IC<sub>50</sub>). The IC<sub>50</sub> values are calculated by plotting the per cent inhibition vs. concentration of compound using EXCEL software for linear regression.

10

15

20

25

30

5

# Selection of 4-oxo-DHO resistant HSV-1 and HSV-2

Vero cells are plated out at a density of 3.5x10<sup>5</sup> cells per well in a six well tissue culture plate. Cells are infected with HSV-1 KOS at a multiplicity of infection (moi) of 0.1 pfu/cell and 1 h post infection the cells are overlayed with 3 ml media containing 20 uM of a 4-oxo-DHQ. Cultures are incubated for 20 h at 37°C, freeze/thawed to release cell-associated virus, and 0.1 ml of culture is used to infect a new monolayer of Vero cells (one passage). Serial passage is repeated seven times in the presence of 20 uM drug. Virus isolates are then plaque purified three times prior to preparation of stocks. Virus recovered from each passage in the presence of compound No. 17 is shown in **Figure 3**. 4-oxo-DHQ resistant HSV-1 and HSV-2 may also be selected by the marker transfer method described below using wild-type HSV DNA and the corresponding mutant HSV polymerase gene.

# Marker Transfer of a HCMV Mutation

A plasmid containing the wild-type HCMV polymerase gene is modified to contain the V823A or V823A and V824L mutations using a site-directed mutagenesis Kit (Stratagene Corp.) and following the manufactures's protocol. HFF cells are plated into T25 tissue culture flasks to achieve 80% confluency at the time of the transfection. Wild type HCMV AD169 DNA and plasmid DNA containing the mutant HCMV polymerase gene are mixed at a ratio of 1:2 (2ug of viral DNA to 4 ug of plasmid DNA). DNA's are transfected using superfect transfection reagent according to methods recommended by the manufacturer (Quiagen Inc.). Cells are harvested five days posttransfection, freeze-thawed to release virus and half of the sample is used to infect HFF cell monolayers. Cells are overlayed with media containing 20 uM 4-oxo-DHQ compound 2 (see Figure 1). Serial

passage is repeated seven times in the presence of 20 uM compound 2 and virus isolates are then plaque purified three times prior to preparation of viral stock.

# Isolation of HSV and HCMV viral DNA

5

10

15

20

30

HSV DNA is purified from the cytoplasm of infected Vero cells. Vero cells (50 % confluent) are infected at an multiplicity of 0.01 PFU/cell. At 3-5 days postinfection infected cells (100% cpe) are harvested by centrifugation at 1000 rpm in a Beckman GS-6R centrifuge. The pelleted cells are resuspended in TE buffer and placed on ice for 15 minutes. NP-40 is then added to a final concentration of 0.2% and incubated on ice for a further 15 minutes. The cells are centrifuged at 2000 rpm for 10 minutes in a Beckman GS-6R centrifuge. The supernatant is removed and EDTA is added to a final concentration of 20 mM followed by the addition of SDS to a final concentration of 0.3% and proteinase K to a concentration of 50 ug/ml then incubated at 45C for 2 hours. HCMV DNA is isolated by infecting HFF cells (25% confluency) with HCMV at an multiplicity of 0.1 PFU/cell. Cells and media are harvested 5-7 days postinfection (100% cpe) and subjected to low speed centrifugation to remove intact cells and cell debris followed by a high speed spin to pellet virus particles (2500 rpm's in a Beckman SW28 rotor for 1 hour). Following incubation of the HSV and HCMV samples, 1.5 volumes of saturated NaI is added to the digested extract and the refractive index is adjusted to 1.434 -1.435. Ethidium bromide is added to a final concentration of 50 ug/ml. The samples are loaded into a VTI 50centrifuge tube and spun for 24 hours at 45,000 rpm. The DNA band is harvested extracted three times with n-butanol, then dialyzed against TE buffer followed by a dialysis against 95% ethanol and a final dialysis against TE buffer.

## 25 DNA Sequencing

HSV-1, HSV-2 or HCMV viral DNA's are sequenced directly using an ABI377 fluorescence sequencer (Perkin Elmer Applied Biosystems, Foster City, CA) and the ABI BigDye PRISMTM dRhodamine Terminator Cycle Sequencing Ready Reaction Kit with AmpliTaq FSTM DNA polymerase (PE Applied Biosystems). Each cycle sequencing reaction contained about 1.0 ug of purified viral DNA. Cycle-sequencing is performed using an initial denaturation at 98°C for 1 min, followed by 50 cycles: 98°C for 30 sec, annealing at 50°C for 30 sec, and extension at 60°C for 4 min. Temperature cycles and times are controlled by a Perkin-Elmer 9700 thermocycler. Extension products are

5

10

15

20

30

purified using CentriflexTM gel filtration cartridges (Edge BioSystems, Gaithersburg, MD). Each reaction product is loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B table top centrifuge) at 750 x g for 1.5 min at room temperature. Column-purified samples are dried under vacuum for about 40 min and then dissolved in 4 ul of a DNA loading solution (83% deionized formamide, 8.3 mM EDTA, and 1.6 mg/ml Blue Dextran). The samples are then heated to 90°C for two min, and held at 4°C until loading. 1.5 ul of each sample is loaded into a single well of the ABI377 sequencer. Sequence chromatogram data files from the ABI377 are analyzed with the computer program Sequencher (Gene Codes, Ann Arbor, MI), for assembly of sequence fragments and correction of ambiguous base calls. Generally sequence reads of 600-700 bp are obtained. Potential sequencing errors are minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers at different locations until all sequencing ambiguities are removed.

The entire coding region of the polymerase genes from both the parent strains and the resistant viruses are sequenced. The DNA sequencing is done using viral DNA as the template thus avoiding cloning of the polymerase genes. The amino acid sequence of the DNA polymerases of HSV-1 KOS, F, Patton and DJL and HSV-2 MS and 186 are compared in **Figure 4**. Amino acids that are identical for the six polymerases are shaded in black while regions where amino acid differences are found are shaded in gray. The amino acid sequence of the four HSV-1 polymerases are essentially identical with only a few minor changes noted between the different HSV-1 strains. The majority of amino acid changes are found when the sequences of the HSV-1 and HSV-2 polymerases are compared.

# 25 <u>Isolation and Characterization of HSV-1 and HSV-2 Mutants That Are Resistant To</u> the 4-oxo-DHQ's and 4-oxo-DHTP Compounds

A panel of viruses consisting of four strains of HSV-1 (KOS, F, DJL, Patton) and three strains of HSV-2 (MS, 35D, 186) are tested in a plaque reduction assay against four different 4-oxo-DHQ compounds (# 1, 2, 4, 5 as shown in Figure 1), and one 4-oxo-DHTP compound (# 3 as shown in Figure 1) and against Acyclovir. The six drugs inhibited replication of the seven virus strains with IC<sub>50</sub> values ranging from 2-10 μM (Table 1). In order to select for 4-oxo-DHQ resistant mutants, HSV-1 strains KOS, F, and DJL along with HSV-2 strains 186 and MS are serially passaged in the presence of 20 uM compound

1. Following the seventh passage, 4-oxo-DHQ resistant virus from each strain are plaque purified three times and high-titer stocks are made. All of the resistant HSV mutants grew to high titers in Vero cells, indicating that the mutations in the resistant isolates did not significantly impair their growth. The mutants selected with 4-oxo-DHQ compound 1 exhibited >10 fold increase in IC<sub>50</sub> when tested in a plaque reduction assay against 4-oxo-DHQ compound 1 Data are shown in Table 2.

Table 2
4-oxo-DHQ Resistant Virus of HSV-1 and HSV-2

Virus Mutants	Compound 1 IC <sub>50</sub> (uM)	Amino Acid Change in HSV DNA Polymerase
HSV-1 Kos-M1	>20	- V823A
HSV-1 F-M1	>20	- V823A
HSV-1 DJL-M1	>20	-V823A
HSV-2 MS-M1	>20	- V826A
HSV-2 186-M1	>20	- V828A

\*HSV-1 and HSV-2 isolates grown in the presence of 4-oxo-DHQ select for resistant virus.

DNA sequence analysis of the 4-oxo-DHQ resistant mutants (HSV-1 KOS-M1, HSV-1 F-M1, HSV-1 DJL-M1, HSV-2 186-M1, HSV-2 MS-M1) demonstrated that all five mutants contained a single point mutation of T to C at the binding domain resulting in a Valine to Alanine amino acid change.

15

20

25

5

# <u>Isolation and Characterization of A HCMV Mutant That Is Resistant to The 4-oxo-</u>DHQ's and 4-oxo-DHTP Compounds

In order to select for a 4-oxo-DHQ HCMV resistant mutant, virus (strain AD169) is serially passaged in the presence of 20 uM a 4-oxo-DHQ. Although we could readily select for HSV mutants using this procedure we failed to isolate an HCMV mutant, even when the virus is passaged at low drug concentrations (<5 uM). Comparison of the amino acid sequence of the HSV polymerase, Y-G-F-T-G-V-Q-H-G, and HCMV polymerase, Y-G-F-T-G-V-V-N-G, in the region of amino acid 823 (underlined amino acid) showed that there is a second valine at position 824 in the HCMV polymerase. In order to determine if both valines need to be changed in order to confer resistance to the 4-oxo-DHQ's, *in vitro* polymerase assays are done using mutant HCMV polymerases containing either V823A or V823A plus V824L (Table 3).

Table 3

HCMV Mutant Polymerase Exhibits Resistance to 4-oxo-DHQ\*

10

15

20

25

Polymerase	Compound 1 IC <sub>50</sub> (uM)
HCMV (wild)	4.6
HCMV V823A	17.2
HCMV V823A/V824L	42.9

<sup>\*</sup>Generation of the valine to alanine at amino acid 823 of HCMV results in a 3.5-fold increase in resistance.

The V823A alone resulted in a 3.5-fold increase in the IC<sub>50</sub> while the polymerase with the double amino acid change had nearly 10-fold increase in the IC<sub>50</sub>. In order to isolate an HCMV resistant mutant marker rescue experiments are done. Plasmids containing the mutant polymerase genes are transfected into HFF cells along with wild type HCMV AD169 DNA. The resulting virus is then serially passaged in the presence of 20 uM compound 1 (see figure 1). A 4-oxo-DHQ resistant virus is isolated from marker rescue studies done with the HCMV polymerase gene containing mutations that result in the V823A, V824L amino acid changes, but not with the gene containing V823A change alone. The mutant selected with compound 1 (HCMV AD169-M1) exhibited ~7-fold increase in IC<sub>50</sub> when tested in a plaque reduction assay compared to Ganciclovir and cidofovir which has a  $\leq$  2-fold change in sensitivity (Table 4).

Table 4
Plaque reduction assay of 4-oxo-DHQ resistant HCMV\*

Drug	HCMV AD169 IC <sub>50</sub> (μM)	HCMV AD169 – M1 IC <sub>50</sub> (μM)
Compound 1	0.7	4.7
Ganciclovir	0.9	1.0
Cidofovir	0.3	0.6

<sup>\*</sup>Recombination of wild-type HCMV with a polymerase gene containing the valine to alanine at amino acid 823 and the valine to leucine at amino acid 824 allowed for selection of resistant virus with about 7-fold less sensitivity to compound 1.

<sup>\*</sup>Mutation of the amino acid from valine to alanine and amino acid 824 from valine to leucine results in an 9-fold increase in resistance, relative to wild type.

<sup>\*</sup>Sensitivity of resistant HCMV virus to Ganciclovir and Cidofovir verifies that the 4-oxo-DHQ's mechanism for inhibiting the polymerase protein is unique

The entire coding region of the HCMV polymerase genes from both the parent strain and the resistant virus are sequenced. The DNA sequencing is again done using viral DNA as the template thus avoiding cloning of the polymerase genes. Comparison of the DNA sequence of the two polymerase genes demonstrated that the resistant mutant contained two point mutations that resulted in the predicted V823A, V824L amino acid changes. As with the HSV resistant viruses these results demonstrate the critical role of the region encompassing amino acid 823 for inhibition of polymerase activity by these compounds.

5

15

20

25

30

# 10 Antiviral Activity of Nucleoside and Non-Nucleoside Polymerase Inhibitors Against 4oxo-DHQ Resistant Mutants

In order to determine if the 4-HQ binding domain mutations alter the sensitivity of the HSV-1, HSV-2 and HCMV mutants to both non-nucleoside (4-oxo-DHQ's) and nucleoside inhibitors (e.g Acyclovir and ganciclovir) several of the mutants are tested in plaque reduction assays against a series of non-nucleoside compounds including Foscarnet (PFA), 4-HQ's 4-oxo-DHQ's and 4-oxo-DHTP's (Table 5). The mutants are also tested against a series of nucleoside inhibitors including acyclovir and ganciclovir (Table 5). The activity of these compounds against the mutants is compared to their activity against the wild type strains that are used to isolate the HSV and HCMV mutants. When tested against a number of 4-HQ's, 4-oxo-DHQ's and 4-oxo-DHTP's and other related classes of compounds all of the drugs are found to inhibit the wild type virus with IC50 values ranging from <0.1 uM to 30 uM. When these drugs are tested against the resistant viruses they are found to have IC<sub>50</sub> values 5 to 10 fold higher then the parent virus. There is little if any difference in the IC50 values of the nucleoside compounds and the non-nucleoside PFA between the wild type and mutant HSV-1, HSV-2, and HCMV viruses. These results demonstrate that the amino acid change in the binding domain (V823A in the HSV-1 polymerase, V826A in the HSV2-MS polymerase, V828A in the HSV2-186 polymerase, and the V823A/V824L changes in the HCMV polymerase) resulted in resistance to the 4oxo-DHQ's and 4-oxo-DHTP's, which provides further evidence that these classes of compounds share an affinity for a region we refer to as the binding domain. In contrast, these amino acid changes did not alter the activity of these viruses to other classes of polymerase inhibitors.

Table 5

Antiviral activity of nucleoside and non-nucleoside polymerase inhibitors against HSV-1, HSV-2, and HCMV Isolates selected for 4-oxo-DHQ resistance\*

		Plaque	e Reduction	a Assay – IC	$C_{50} (\mu M)$	
Drug	HSV-2 MS	HSV-2 MS-M1	HSV-1 KOS	HSV-1 KOS-M1	HCMV AD169	HCMV AD169-M1
6	28.8	>50	24.6	>50	5.1	>16
7	8.8	27.9	6.5	>50	0.3	3.4
8	2.3	>50	5.1	>50	<0.1	1.1
9	0.9	48.7	1.9	>50	<0.1	3.1
10	29.2	>50	15.8	>50	1.1	>16
11	3.0	>50	3.1	>50	0.7	3.9
12	0.4	12.5	1.3	>50	0.2	1.1
13	5.3	>50	5.5	<25	2.7	>16
14	1.6	>50	28.4	>50	0.9	18.4
2	1.3	>50	3.3	>50	0.4	4.0
4	2.1	28.4	4.2	>50	0.6	2.1
3	0.8	>50	4.0	>50	1.5	6.2
15	5.9	>50	>50	>50	0.7	7.7
Iudr	5.0	6.1	1.1	0.8	ND	ND
Bvdu	5.8	5.9	2.1	0.1	ND	ND
ACV	2.4	2.8	3.9	4.4	ND	ND
AraC	0.2	0.1	0.2	0.2	ND	ND
AraT	6.6	3.6	11.6	3.6	ND	ND
AraA	10.6	18.2	26.1	27.2	ND	ND
GCVir	ND	ND	ND	ND	0.8	0.8
CDV	ND	ND	ND	ND	0.4	0.3
PFA	ND	ND	ND	ND	38	<20

<sup>5 \*</sup>HSV-2 MS, HSV-1 KOS, HCMV AD169: wild type strains

10

15

Antiviral compounds identified by the present invention can conveniently be administered in a pharmaceutical composition containing the compound in combination with a suitable excipient, the composition being useful in combating viral infections. Pharmaceutical compositions containing a compound appropriate for antiviral use are prepared by methods and contain excipients which are well known in the art. A generally recognized compendium of such methods and ingredients is Remington's Pharmaceutical Sciences by E.W. Martin (Mark Publ. Co., 15th Ed., 1975).

Antiviral compounds identified by the present invention and their compositions can be administered parenterally (for example, by intravenous, intraperitoneal or intramuscular

<sup>\*</sup>HSV-2 MS-M1, HSV-1 KOS-M1, HCMV AD169-M1: mutants selected for 4-oxo-DHQ resistance \*ND – Not Done.

5

10

15

20

25

30

injection), topically, orally, or rectally, depending on whether the preparation is used to treat internal or external viral infections.

For oral therapeutic administration, the active compound may be combined with one or more excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2 to about 60% of the weight of a given unit dosage form. The amount of active compound in such therapeutically useful compositions is such that an effective dosage level will be obtained.

The tablets, troches, pills, capsules, and the like may also contain the following: binders such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a lubricant such as magnesium stearate; and a sweetening agent such as sucrose, fructose, lactose or aspartame or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring may be added. When the unit dosage form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier, such as a vegetable oil or a polyethylene glycol. Various other materials may be present as coatings or to otherwise modify the physical form of the solid unit dosage form. For instance, tablets, pills, or capsules may be coated with gelatin, wax, shellac or sugar and the like. A syrup or elixir may contain the active compound, sucrose or fructose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any unit dosage form should be pharmaceutically acceptable and substantially non-toxic in the amounts employed. In addition, the active compound may be incorporated into sustained-release preparations and devices.

Antiviral compounds identified by the present invention and their compositions can also be administered intravenously or intraperitoneally by infusion or injection. Solutions of the active compound or its salts can be prepared in water, optionally mixed with a nontoxic surfactant. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, triacetin, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

Pharmaceutical dosage forms suitable for injection or infusion can include sterile aqueous solutions or dispersions or sterile powders comprising the active ingredient which

5

10

15

20

25

30

are adapted for the extemporaneous preparation of sterile injectable or infusible solutions or dispersions, optionally encapsulated in liposomes. In all cases, the ultimate dosage form should be sterile, fluid and stable under the conditions of manufacture and storage. The liquid carrier or vehicle can be a solvent or liquid dispersion medium comprising, for example, water, ethanol, a polyol (for example, glycerol, propylene glycol, liquid polyethylene glycols, and the like), vegetable oils, nontoxic glyceryl esters, and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the formation of liposomes, by the maintenance of the required particle size in the case of dispersions or by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, buffers or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filter sterilization. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze drying techniques, which yield a powder of the active ingredient plus any additional desired ingredient present in the previously sterile-filtered solutions.

For topical administration, the present compounds may be applied in pure form, i.e., when they are liquids. However, it will generally be desirable to administer them to the skin as compositions or formulations, in combination with a dermatologically acceptable carrier, which may be a solid or a liquid.

Useful solid carriers include finely divided solids such as talc, clay, microcrystalline cellulose, silica, alumina and the like. Useful liquid carriers include water, alcohols or glycols or water-alcohol/glycol blends, in which the present compounds can be dissolved or dispersed at effective levels, optionally with the aid of non-toxic surfactants. Adjuvants such as fragrances and additional antimicrobial agents can be added to optimize the properties for a given use. The resultant liquid compositions can be applied from absorbent pads, used to impregnate bandages and other dressings, or sprayed onto the affected area using pump-type or aerosol sprayers. Thickeners such as synthetic polymers, fatty acids,

fatty acid salts and esters, fatty alcohols, modified celluloses or modified mineral materials can also be employed with liquid carriers to form spreadable pastes, gels, ointments, soaps, and the like, for application directly to the skin of the user.

Examples of useful dermatological compositions which can be used to deliver the compounds of formula I to the skin are known to the art; for example, see Jacquet et al. (U.S. Pat. No. 4,608,392), Geria (U.S. Pat. No. 4,992,478), Smith et al. (U.S. Pat. No. 4,559,157) and Wortzman (U.S. Pat. No. 4,820,508).

5

10

15

20

25

30

Useful dosages of the compounds of formula I can be determined by comparing their *in vitro* activity, and *in vivo* activity in animal models. Methods for the extrapolation of effective dosages in mice, and other animals, to humans are known to the art; for example, see U.S. Pat. No. 4,938,949.

The compound is conveniently administered in unit dosage form; for example, containing 5 to 1000 mg, conveniently 10 to 750 mg, most conveniently, 50 to 500 mg of active ingredient per unit dosage form. The desired dose may conveniently be presented in a single dose or as divided doses administered at appropriate intervals, for example, as two, three, four or more sub-doses per day. The sub-dose itself may be further divided, e.g., into a number of discrete loosely spaced administrations; such as multiple inhalations from an insufflator or by application of a plurality of drops into the eye.

For internal infections, the compositions can be administered orally or parenterally at dose levels, calculated as the free base, of about 0.1 to 300 mg/kg, preferably 1.0 to 30 mg/kg of mammal body weight, and can be used in man in a unit dosage form, administered one to four times daily in the amount of 1 to 1000 mg per unit dose.

For parenteral administration or for administration as drops, as for eye infections, the compounds are presented in aqueous solution in a concentration of from about 0.1 to about 10%, more preferably about 0.1 to about 7%. The solution may contain other ingredients, such as emulsifiers, antioxidants or buffers.

Generally, the concentration of the compound(s) of formula I in a liquid composition, such as a lotion, will be from about 0.1-25 wt-%, preferably from about 0.5-10 wt-%. The concentration in a semi-solid or solid composition such as a gel or a powder will be about 0.1-5 wt-%, preferably about 0.5-2.5 wt-%.

The exact regimen for administration of the compounds and compositions disclosed herein will necessarily be dependent upon the needs of the individual subject being treated, the type of treatment and, of course, the judgment of the attending practitioner.

The antiviral activity of a compound of the invention can be determined using pharmacological models which are well known to the art, or using Test A described below.

The compounds of formula (I) and pharmaceutically acceptable salts thereof are useful as antiviral agents. Thus, they are useful to combat viral infections in animals, including man. The compounds are generally active against herpes viruses, and are particularly useful against the varicella zoster virus, the Epstein-Barr virus, the herpes simplex virus, the human herpes virus type 8 (HHV-8) and the cytomegalovirus (CMV).

10

#### **CLAIMS**

## We claim:

1. A method of selecting compounds that inhibit herpes viruses comprising:

- a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type herpes virus,
- b) measuring  $IC_{50}$  of the same compound that inhibits a binding domain mutant herpes virus which is the same strain as the wild type herpes virus,
  - c) comparing  $IC_{50}$  of step a with  $IC_{50}$  of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.

10

- 2. A method of selecting compounds that inhibit herpes viruses comprising:
- a) measuring IC<sub>50</sub> of a compound of interest that inhibits a binding domain mutant herpes virus,
- b) measuring IC<sub>50</sub> of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus,
  - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step a is at least 3 times greater than the  $IC_{50}$  of step b.
- 20 3. The method of claim 1 or 2 wherein the herpes virus is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.
  - 4. A method of selecting compounds that inhibit herpes viruses comprising:
  - a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type HSV-1,
- 25 b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant HSV-1 which is the same strain as the wild type herpes virus,
  - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.

- 5. A method of selecting compounds that inhibit herpes viruses comprising:
- a) measuring  $IC_{50}$  of a compound of interest that inhibits a binding domain mutant HSV-1,

b) measuring IC<sub>50</sub> of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant HSV-1,

- c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
- d) selecting the compound of interest wherein the  $IC_{50}$  of step a is at least 3 times greater than the  $IC_{50}$  of step b.
  - 6. The method of claim 4 or 5 wherein HSV-1 is HSV-1 KOS, HSV-1 F, HSV-1 DJL or HSV-1 Patton.
- 7. The method of claim 5 or 6 wherein the mutation of a wild type herpes virus to mutant herpes virus is at amino acid 823 from valine to alanine.
  - 8. A method of selecting compounds that inhibit herpes viruses comprising:
  - a) measuring  $IC_{50}$  of a compound of interest that inhibits a wild type HSV-2,
- 15 b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant HSV-2 which is the same strain as the wild type herpes virus,
  - c) comparing  $IC_{50}$  of step a with  $IC_{50}$  of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.

20

- 9. A method of selecting compounds that inhibit herpes viruses comprising:
- a) measuring  $IC_{50}$  of a compound of interest that inhibits a binding domain mutant HSV-2,
- b) measuring IC<sub>50</sub> of the same compound that inhibits a wild type herpes virus which is the same strain as the mutant HSV-2,
  - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
  - d) selecting the compound of interest wherein the  $IC_{50}$  of step a is at least 3 times greater than the  $IC_{50}$  of step b.
- 30 10. The method of claim 8 or 9 wherein HSV-2 is HSV-2 MS, HSV-2 35D, or HSV-2 186.
  - 11. A method of selecting compounds that inhibit herpes viruses comprising:

a) measuring IC<sub>50</sub> of a compound of interest that inhibits a wild type HCMV,

- b) measuring IC<sub>50</sub> of the same compound that inhibits a binding domain mutant HCMV which is the same strain as the wild type herpes virus,
- c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and
- selecting the compound of interest wherein the  $IC_{50}$  of step b is at least 3 times greater than the  $IC_{50}$  of step a.
  - 12. A method of selecting compounds that inhibit herpes viruses comprising:
  - a) measuring IC<sub>50</sub> of a compound of interest that inhibits a binding domain mutant HCMV,
    - b) measuring IC<sub>50</sub> of the same compound that inhibits a wild type herpes virus which is the same strain of the mutant HCMV,
    - c) comparing IC<sub>50</sub> of step a with IC<sub>50</sub> of step b; and

- d) selecting the compound of interest wherein the IC<sub>50</sub> of step a is at least 3 times greater than the IC<sub>50</sub> of step b.
  - 13. The method of claim 8 or 9 wherein HCMV is AD169.
- 14. The methods of claims 1, 4, 8, or 11 wherein  $IC_{50}$  of step b is at least 5 times greater than the  $IC_{50}$  of step a.
  - 15. The methods of claims 2, 5, 9, or 12 wherein  $IC_{50}$  of step a is at least 5 times greater than the  $IC_{50}$  of step b.
- 25 16. A use of compounds for manufacturing of medicinals for selectively treating diseases caused by herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein said compound inhibits herpes viruses by interaction with the binding domain in the viral DNA polymerase.
- A use of compounds for manufacturing of medicinals for selectively inhibiting herpes viruses in a human host comprising administering a compound to a human in need of such treatment wherein IC<sub>50</sub> of the compound that inhibits a binding domain

mutant herpes virus is at lease 3 times greater than  $IC_{50}$  of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.

18. The use of claim 17 wherein  $IC_{50}$  of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than  $IC_{50}$  of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes viruse.

- 19. The use of claim 17 wherein herpes viruses is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8.
- A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein IC<sub>50</sub> of the compound that inhibits a binding domain mutant herpes virus is at lease 5 times greater than IC<sub>50</sub> of the compound that inhibits a wild type herpes virus which is the same strain as the mutant herpes virus.
- A use of compounds for manufacturing of medicinals for treating herpesviral infections in a human host wherein said compound inhibits the herpesvirus by interacting with the binding domain in the viral DNA polymerase.
  - 22. The herpesviral infection of claim 20 or 21 which is HSV-1, HSV-2, HCMV, VZV, EBV, or HHV-8 infection.
- 23. A compound for the inhibiting of herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results a change of the wild type HSV-1 polymerases at amino acid 823 from valine to alanine.
- 24. A compound for inhibiting herpesvirus DNA polymerases wherein passage of a wild type herpes virus in the presence of said compound results in a change of the wild type HCMV polymerases at amino acid 823 from valine to alanine and at amino acid 824 from valine to leuline.

25. A mutant herpesvirus DNA molecule having a nucleotide sequence selected from a group consisting of SEQ.ID.NO. 1; SEQ.ID.NO. 3; SEQ.ID.NO. 5; SEQ.ID.NO. 7; SEQ.ID.NO. 9; and SEQ.ID.NO. 11.

A mutant herpesvirus polymerase amino acid molecule having an amino acid sequence selected from a group consisting of SEQ.ID.NO. 2; SEQ.ID.NO. 4; SEQ.ID.NO. 6; SEQ.ID.NO. 8; SEQ.ID.NO. 10 and SEQ.ID.NO. 12.

Figure 1 4-HQ, 4-oxo-DHQ and 4-oxo-DHTP antiviral compounds

Compound No. 5

# (Figure 1 continue)

# Compound No. 7

# (Figure 1 continue)

(Figure 1 continue)

**Compound No.15** 

Compound 17

Figure 2. The HSV1 (KOS Strain) DNA Polymerase Amino Acid 823 is Critical for Resistance to 4-Hydroxyquinolines and Related Compounds

ı۱	/ A		II	٧	i	Ш		ı	]	V	
NH-		_		_	<b>.</b>		<b>I</b> —			<b></b>	<del>⊣</del> соон
		_			_	Т		_		-	
					1	V823	3A				
							- 1				
	HSV1-KOS-M1	Υ	G	F	Т	G	Α	Q	н	G - 826	
	HSV1	·Y	G	F	T	G	٧	Q	Н	G - 826	
	HSV2	Y	G	F	T	G	V	Q	Н	G - 829	
	VZV	Υ	G	F	T	G	V	Α	Q	G - 791	
	EBV	Υ	G	F	Т	G	٧	Α	N	G - 696	
	HCMV	Υ	G	F	Т	G	V	٧	Ν	G - 826	
	HHV6	Υ	G	V	Т	G	Α	Α	Н	G - 681	
	HHV7	Υ	G	V	Т	G	Α	T	Н	S - 681	
	HHV8	Y	G	F	Т	G	٧	Α	S	G - 696	

Schematic of HSV1 polymerase illustrating the conserved regions A and I-VI found in class 2 polymerases. Also shown are the amino acid sequence for the highly conserved herpesvirus domain in region III which surrounds the HSV1 amino acid 823.

Figure 3 Serial Passage of HSV-1 in Presence of 20 μM compound 17

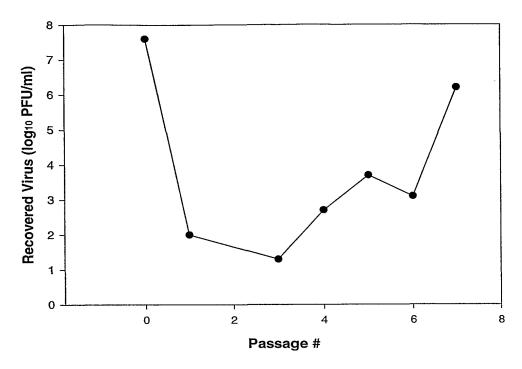


Figure 4 Comparison of Wild type HSV-1 and HSV-2 DNA Polymerases Amino Acid Sequences Alligned by Amino Acid Homology\*

		J					•
	HSV2-MS	MECAACCOTC	PCCKSAARAA	SGFFAPHNPR	GATOTAPPPC	RRQNFYNPHL	-50
		MEGAAGGIA	DOOKOM ADAA	CCEEN DUNIDD	CAMOMADDDC	RRQNFYNPHL	-50
	HSV2-186	MECAAGGPAS	PGGKSAARAA	SGFFAPHNPK	GATQTAPPPC	KKÖNLIMEUD	-30
5	HSV1-Kos	MFSGGGGPLS	PGGKSAARAA	SGFFAPAGPR	GAGR.GPPPC	LRQNFYNPYL	-49
	HSV1-Patton	MESCCCCPLS	PGGKSAARAA	SGFFAPAGPR	GAGR.GPPPC	LRQNFYNPYL	-49
		MECCOCCIES	DCCKCAADAA	CCEEVDYCDD	CACE CEPEC	LRQNFYNPYL	-49
	HSV1-DJL	MESGGGETIS	PGGKSAAKAA	SGFFAFAGFK	GAGR.GFFFC	DIOMETRICAL TO	40
	HSV1-F	MFSGGGGPLS	PGGKSAARAA	SGFFAPAGPR	GAGR.GPPPC	LRQNFYNPYL	-49
					201 222 222	ODECUIDODI	100
10	HSV2-MS	AQTGTQPKAP	GPAQRHTYYS	ECDEFRFIAP	RSLDEDAPAE	QRTGVHDGRL	-100
	HSV2-186	AOTGTOPKAP	GPAORHTYYS	ECDEFRFIAP	RSLDEDAPAE	QRTGVHDGRL	-100
	HSV1-Kos	A DY/CTOOK DT	CDTOPHTVVC	ECDEFRETAP	RVIDEDAPPE	KRAGVHDGHL	-99
		AFVGIQQILI	GFTQMITTID	ECDELIII III	DAT DEDY DDE	KRAGVHDGHL	_00
	HSV1-Patton	APVGTQQKPT	GPTQRHTYYS	ECDEFREIAP	RVLDEDAPPE	KKAGVADGAL	-99
	HSV1-DJl	APVGTQQKPT	GPTQRHTYYS	ECDEFRFIAP	RVLDEDAPPE	KRAGVHDGHL	-99
15	HSV1-F	APVGTQQKPT	GPTQRHTYYS	ECDEFRFIAP	RVLDEDAPPE	KRAGVHDGHL	-99
	HSV2-MS	RRAPKVYCGG	DERDVLRVGP	EGFWPRRLRL	WGGADHAPKG	FDPTVTVFHV	-150
	HSV2-186	BB Z DKI/VCGG	DEBUMURAGE	EGEWPRRLRL	WGGADHAPEG	FDPTVTVFHV	-150
		TOTAL TOTAL	DEDDIT DUCC	CCEMPDDCDI	MCCADAYDYC	FNPTVTVFHV	_1/9
	HSV-Kos	KRAPKVICGG	DERDVLRVGS	GGEWEKKSKU	WGGVDIAFAG	TIVE TO TOTAL	1.40
20	HSV1-Patton	KRAPKVYCGG	DERDVLRVGS	GGFWPRRSRL	WGGVDHAPAG	FNPTVTVFHV	-149
	HSV1-DJL	KRAPKVYCGG	DERDVLRVGS	GGFWPRRSRL	WGGVDHAPAG	FNPTVTVFHV	-149
		KD & DKI WCCC	DEBDAT BACK	CCEMPPDCDI.	WCCVDHADAG	FNPTVTVFHV	_149
	HSV1-F	KRAPKVICGG	DEKDATIKAGS	GGEWEKKDILD	WGGADIMI NG	TIMETOTOTIO	J. 1
	HSV2-MS	VDTI.EHUEHA	VCMDAAOLHE	REMDATTPAG	TVTTTTGTTP	EGHRVAVHVY	-200
0.5		TDTREETARIN	TOTALVACUIT	TOTAL TOTAL	TVIIDICITI	ECHDIVATURA	200
25	HSV2-186	ADIPEHAEHY	YSMRAAQLHE	REMDATTPAG	TATTFRETTE	EGHRVAVHVY	-200
	HSV-Kos	YDILENVEHA	YGMRAAQFHA	RFMDAITPTG	$ ext{TVITLLGLTP}$	EGHRVAVHVY	-199
	HSV1-Patton	VDTLEMMEHA	YGMRAAOFHA	REMDATTETG	TVITLLGLTP	EGHRVAVHVY	-199
		TOTT TONT TOTAL	ACMEN A VERIN	DEMINA LUDUC	ጥህፓጥፒፒርፒጥ፬	EGHRVAVHVY	-199
	HSV1-DJL	ADTPENARHY	YGMRAAQFHA	KEMDAITEIG	IVIIDEGETE	EGIIKVAVIIVI	100
	HSV1-F	YDILENVEHA	YGMRAAQFHA	RFMDAITPTG	TVTTLLLGLTP	EGHRVAVHVY	-199
30							0.5.0
	HSV2-MS	GTRQYFYMNK	AEVDRHLQCR	APRDLCERLA	AALRESPGAS	FRGISADHFE	-250
	HSV2-186	GTROVEYMNK	AEVDRHLOCK	APRDLCERLA	AALRESPGAS	FRGISADHFE	-250
		OTTIQIT TIMIT	EEADDIII OOD	A DDDI CEDMA	A A T. DECDCA C	FRGISADHFE	-249
	HSV-Kos	GIROIFIMMK	FEADKUDGCK	APROLUCERMA	CADICAMIAN	PROTONDITE	240
	HSV1-Patton	GTRQYFYMNK	EEVDRHLQCR	APROLCERMA	AALRESPGAS	FRGISADHFE	-249
35	HSV1-DJL	GTROYFYMNK	EEVDRHLOCR	APRDLCERMA	AALRESPGAS	FRGISADHFE	-249
	HSV1-F	GTRQYFYMNK	EEVDRHLQCR	APRDLCERMA	AALRESPGAS	FRGISADHFE	-249
	HSV2-MS	AEVVERADVY	YYETRPTLYY	RVFVRSGRAL	AYLCDNFCPA	IRKYEGGVDA	-300
	HSV2-186	$\Delta E(X)EE\Delta D(Y)$	YYETR PTI,YY	RVFVRSGRAL	AYLCDNFCPA	IRKYEGGVDA	-300
40		EVVERTDVY Y		TATE CODITE C	VI CDNECDA T	KKAEGGIUV	-299
40		EVVERTDVY Y	AETKEAPEA K	VIVRSGRVL S	APCDIARCEM T	KKIEGG V DA	
	HSV1-Patton	AEVVERTDVY	YYETRPALFY	RVYVRSGRVL	SYLCDNFCPA	IKKYEGGVDA	-299
	HSV1-DJL	*AEWERTDWY	YYETRPALFY	RVYVRSGRVL	SYLCDNFCPA	IKKYEGGVDA	-299
	HSV1-F	AEVVERTOVY	YYETRPALFY	RVYVRSGRVL	SYLCDNFCPA	IKKYEGGVDA	-299
	110 1 1						
45	HSV2-MS	TTRFTLDNPG	FVTFGWYRLK	PGRGNAPAOP	RPPTAFGTSS	DVEFNCTADN	-350
15	HSV2-186	DEDELI DADO	ETTECHTVDT K	DCDCNIA DA OD	PDDTAFGTGG	DVEFNCTADN	-350
		TIRE LEDNING	FATEGMININ	- FOLGIVATAÖT	KITIAFGIBB	DVEENOENDN	240
	HSV-Kos	TTRFILDNPG	FVTFGWYRLK	PGRNNTLAQP	RAPMARGISS	DVEFNCTADN	-349
	HSV1-Patton	TTRFILDNPG	FVTFGWYRLK	PGRNNTLAOP	RAPMAFGTSS	DVEFNCTADN	-349
	HSV1-DJL	MADELI DADO	ETMECTATOR R		PADMAFGTSS	DVEFNCTADN	-349
		TIKETDDMEG	FVIFGWIRE	DODAMAT TOTAL		DATE NO CONTRACTOR	3 4 0
50	HSV1-F	TTRFILDNPG	F.A.I.F.GMAKTR	. PGRNN'I LAQP	RAPMARGISS	DVEFNCTADN	-343
				Darr canner	A ELECTIVE COLUMN	TTTOTCOLLY	400
	HSV2-MS	LAVEGAMCDL	PAYKTWCFDI	ECKAGGEDEL	AFPVAEKPED	LVIQISCLLY	-400
	HSV2-186	LAVEGAMCDL	PAYKLMCFDI	ECKAGGEDEL	AFPVAERPED	LVIQISCLLY	-400
	HSV-Kos	TATECCMODE	PAYKIMCFDT	ECKAGGEDET	AFPVAGHPED	LVIQISCLLY	-399
		TWTTGGWGDU	DAZINI MODDI		מים מנוט אנוסים א	LVIQISCLLY	_300
55	HSV1-Patton	LAIEGGMSDL	PAYKUMCEDI	ECKAGGEDEL	AFPVAGRPEL	TATOTOCHHI	-322
	HSV1-DJL	LAIEGGMSDL	PAYKLMCFDI	ECKAGGEDEL	AFPVAGHPED	LVIQISCLLY	-399
	HSV1-F	LAIEGGMSDL	PAYKLMCFDI	ECKAGGEDEL	AFPVAGHPED	LVIQISCLLY	-399
	HSV2-MS	DLSTTALEHT	LLFSLGSCDL	PESHLSDLAS	RGLPAPVVLE	FDSEFEMLLA	-450
60		DI CHIMAT DITT	TIPOTOCODI	DECUT COT AC	י דותוס גים ובים	FDSEFEMLLA	-450
60	HSV2-186	DESTITATERT	. חחנטהפכחד	· TEOUTOUTY	, TOTEMENATE		110
	HSV-Kos	DLSTTALEHV	LLFSLGSCDL	PESHLNELA	A RGLPTPVVLE	FDSEFEMLLA	-449
	HSV1-Patton	DLSTTALEHV	LLFSLGSCDL	PESHLNELA	RGLPTPVVLE	FDSEFEMLLA	-449
	HSV1-DJL	DI GOMAT DIN	T.T.RST.CSCDT	DESHINET AZ	RCLPTPIALE	FDSEFEMLLA	-449
		DI COURT I FILLY	TIECT CCCTT	DEGLERAMENS	TOTITION TO	PDCEFFMILLY	_4.49
	HSV1-F	DLSTTALEHV	TITESTGSCDI	· LESHTMETW	7 KGTLILAATE	FDSEFEMLLA	
65							

	HSV2-MS HSV2-186	FMTFVKOYGP	EFVTGYNIIN	FDWPFVLTKL	TEIYKVPLDG TEIYKVPLDG	YGRMNGRGVF	-500
~	HSV-Kos HSV1-Patton	FMTLVKOYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG TDIYKVPLDG TDIYKVPLDG	YGRMNGRGVF	<del>, 4</del> 99
5	HSV1-DJL HSV1-F	FMTLVKQYGP	EFVTGYNIIN	FDWPFLLAKL	TDIYKVPLDG	YGRMNGRGVF	- <b>4</b> 99
	HSV2-MS HSV2-186	RVWDIGOSHF	OKRSKIKVNG	MVNIDMYGII	TDKVKLSSYK TDKVKLSSYK	LNAVAEAVLK	-550
10	HSV-Kos	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK TDKIKLSSYK	LNAVAEAVLK	-549 -549
	HSV1-Patton HSV1-DJL	RVWDIGQSHF	OKRSKIKVNG	MVNIDMYGII	TDKIKLSSIK	LNAVAEAVLK	-549
	HSV1-F	RVWDIGQSHF	QKRSKIKVNG	MVNIDMYGII	TDKIKLSSYK	LNAVAEAVLK	-549
15	HSV2-MS	DKKKDLSYRD	IPAYYASGPA	QRGVIGEYCV	QDSLLVGQLF	FKFLPHLELS	-600
	HSV2-186 HSV-Kos	DKKKDLSYRD	TDAVVAACDA	ORGVIGEYCV	QDSLLVGQLF QDSLLVGQLF	FKFLPHLELS	-599 ·
	HSV1-Patton.	DKKKDLSTRD	IPAYYAAGPA	ORGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
	HSV1-DJL	DKKKDLSYRD	IPTYYAAGPA	QRGVIGEYCI	QDSLLVGQLF	FKFLPHLELS	-599
20	HSV1-F				QDSLLVGQLF		
	HSV2-MS	AVARLAGINI	TRTIYDGQQI	RVFTCLLRLA	GQKGFILPDT	QGRFRGLDKE	-650
	HSV2-186	AVARLAGINI	TRTIYDGQQI	RVFTCLLRLA	GQKGFILPDT DQKGFILPDT	QGRFRGLDKE	-650 -649
25	HSV-Kos HSV1-Patton	AVARLAGINI	J.K.T.T.X.D.G.O.O.T.	RALLCTPRTY	DQKGFILPDT	OGRERGAGGE	-649
23	HSV1-DJL	AVARLAGINI	TRTIYDGOOI	RVFTCLLRLA	DQKGFILPDT	QGRFRGAGGE	-649
	HSV1-F	AVARLAGINI	TRTIYDGQQI	RVFTCLLRLA	DQKGFILPDT	QGRFRGGGGE	-649
	HSV2-MS	APKRPAVPRG	EGERPGDGNG	DEDKDDDE	DEDGDERE.E	VARETGGRHV	-697
30	HSV2-186				DEDGDERE.E	VARETGGRHV	-697
	HSV-Kos		DEERP		EEGGGEREPE		
	HSV1-Patton	APKRPAAARE	DEERP	EEEGEDEDER	EEGGGEREPE EEGGGEREPE	CARETAGRAV	-694
	HSV1-DJL HSV1-F	APKKPAAARE	DEEKP	EEEGEDEDER	EEGGGEREPE	GARETAGRHV	-694
35	UPAT-6	AFINEAAANE	DEEKE		PECCOLICE E		
	HSV2-MS	GYQGARVLDP	TSGFHVDPVV	VFDFASLYPS	IIQAHNLCFS	TLSLRPEAVA	-747
	HSV2-186	GYQGARVLDP	TSGFHVDPVV	VFDFASLYPS	IIQAHNLCFS	TLSLRPEAVA	-749
	HSV-Kos	GYQGARVLDP	TSGFHVNPVV	VFDFASLYPS	IIQAHNLCFS	TLSLRADAVA	-744
40	HSV1-Patton	GYQGARVLDP	ISGFHVNPVV		IIQAHNLCFS IIQAHNLCFS		
40	HSV1-DJL HSV1-F	GYOGARVLDP	TSGFTVNPVV	VEDEASLIES	IIQAHNLCFS	TLSLRADAVA	-744
	HPAT-L						
	HSV2-MS	HLEADRDYLE	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-797
	HSV2-186	HLEADRDYLE	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-/99 704
45	HSV-Kos	HLEAGKDYLE	TEACCEDE EE	VKAHVRESLL	SILLRDWLAM SILLRDWLAM	RKOTRSRIPO	-794 -794
	HSV1-Patton HSV1-DJL	HLEAGKDYLE	TEVGGRRLFF	VKAHVRESLI	SILLRDWLAM	RKOIRSRIPO	-794
	HSV1-F	HLEAGKDYLE	IEVGGRRLFF	VKAHVRESLL	SILLRDWLAM	RKQIRSRIPQ	-794
50	HSV2-MS	C.T.WARROWS	KOOAATKVVC	NSVYGFTGVO	HGLLPCLHVA	ATVTTIGREM	-847
50	HSV2-186	SPPEEAVLLD	KOOAAIKVVC	NSVYGFTGVQ	HGLLPCLHVA	ATVTTIGREM	-849
	HSV-Kos	SSPEEAVLLD	KOQAAIKVVC	NSVYGFTGVQ	HGLLPCLHVA	ATVTTIGREM	-844
	HSV1-Patton	SSPEEAVLLD	KQQAAIKVVC	NSVYGFTGVQ	HGLLPCLHVA	ATVTTIGREM	-844
	HSV1-DJL	SSPEEAVLLD	KQQAAIKVVC	NSVYGFTGVQ	HGLLPCLHVA	ATVTTIGREM	-844
55	HSV1-F				HGLLPCLHVA		
	HSV2-MS	LLATRAYVHA	RWAEFDQLLA	DFPEAAGMRA	PGPYSMRIIY	GDTDSIFVLC	-897
	HSV2-186	LLATRAYVHA	RWAEFDQLLA	DEPEAAGMRA	. PGPYSMRIIY . PGPYSMRIIY	GDADGIEALC	-099 -091
60	HSV-Kos HSV1-Patton	LLATKEYVHA	АЛЛОЧЧААМЯ К.Т.ТОЧЧААМЯ	DEDEVADMEN	PGPYSMRIII PGPYSMRIIY	GDTDSTFVLC	-89 <b>4</b>
UU	HSV1-Patton	TLATREVVHA	RWAAFEOLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
	HSV1-F	LLATREYVHA	RWAAFEQLLA	DFPEAADMRA	PGPYSMRIIY	GDTDSIFVLC	-894
	HSV2-MS	RGLTAAGLVA	MGDKMASHIS	RALFLPPIKI	ECEKTFTKLL	LIAKKKYIGV	-947
65	HSV2-186	RGLTAAGLVA	MGDKMASHIS	RALFLPPIKI	ECEKTFTKLL	LIAKKKYIGV	-949
	HSV-Kos	RGLTAAGLTA	MGDKMASHIS	RALFLPPIKI	ECEKTFTKLL	LIAKKKYIGV	-944 011
	HSV1-Patton	RGLTAAGLTA	MGDKMASHIS	KALLLELIKI	. ECEKTFTKLL	TTAKKKATGA	- 244

	HSV1-DJL	RGLTAAGLTA	VGDKMASHIS	RALFLPPIKL	ECEKTFTKLL	LIAKKKYIGV	-944
	HSV1-F	RGLTAAGLTA	VGDKMASHIS	RALFLSPIKL	ECEKTFTKLL	LIAKKKYIGV	-944
	HSV2-MS	TCGGKMLTKG	VDLVRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	<del>-</del> 997
5	HSV2-186	TCGGKMLTKG	VDLVRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	-999
_	HSV-Kos	TYGGKMLTKG	VDLVRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	-994
	HSV1-Patton	TYGGKMLTKG	VDLVRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	-994
	HSV1-DJL	TAGGRMITEG	VDLVRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	-994
	HSV1-F	TACCKMLTAC	VDI.VRKNNCA	FINRTSRALV	DLLFYDDTVS	GAAAALAERP	-994
10	IID A T T.	TIOCITATION	ADD ALUGINGIA	1 224142 22 22 2			
10	HSV2-MS	ス ぱ ぽ い	FCI.OAFGAM.	VDAHRRTTDP	ERDIQDFVLT	AELSRHPRAY	-1047
	HSV2-MS	ADDIVIDANT DE LE	EGLOAFGAVI.	VDAHERTTDE	ERDIQDFVLT	AELSRHPRAY	-1049
	HSV-Kos	AREWIAKELE	ECLONECAVI.	VDAHRRITDI	ERDIQDFVLT	AELSRHPRAY	-1044
	HSV1-Patton	ADDWIANTLE D	EGLONEGAVI.	VDAHRRTTDI	ERDIQDFVLT	AELSRHPRAY	-1044
15	HSV1-DJL	ACCMUAREDE D	EGLOAFGAVI.	MUNICALDI	ERDIQDFVLT	AELSRHPRAY	-1044
13		ADDWIT ADDID	EGUQAEGAVI	OUNTAGETUDD	ERDIQDFVLT	AELSRHPRAY	-1044
	HSV1-F	AEEWLARPLP	EGLQAFGAVL	ADMUNTIDE	EKDIQDI VIII	Mindidition	2011
	**************************************		******* <b>M</b>	TADCTADDALDA	VIVAQTREVE	ETTIADI.AAT.R	-1097
	HSV2-MS	TNKRLAHLTV	YYKLMARRAQ	ABSTUDITED	VIVAQTREVE	ETVARDAGER	-1099
00	HSV2-186	TNKRLAHLTV	YYKLMARRAQ	ABSIVDKILI	VIVAQTREVE	ET AVIDAGEN	-1094
20	HSV-Kos	TNKRLAHLTV	YYKLMARRAQ	VPSIKDRIPI	VIVAQTREVE	EIVANDAADIN	_1094
	HSV1-Patton	TNKRLAHLTV	YYKLMARRAQ	VPSINDRIPI	VIVAQTREVE	ET VAICHAALIK	-1094
	HSV1-DJL	TNKRLAHLTV	YYKLMARRAQ	VPSIKDRIPY	VIVAQTREVE	EIVARLIAALK	-1094
	HSV1-F	TNKKLAHLT.V	YYKLMARRAQ	ABSIKDKIBI	VIVAQIREVE	EIVANDANDIN	-1024
0.5			~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	A TYD DD DODD CII	ADPPGGASKP	DET.TATCET.AE	-1117
25	HSV2-MS	ELDAAAPGDE	PAPPAALPSP	AKKPKETPSI	ADPPGGASKP	DELL'AGELYE	_11/19
	HSV2-186	ELDAAAPGDE	PAPPAALPSP	AKRPRETPSH	ADPPGGASKP	KKLLVSELAE	_111/
	HSV-Kos	ELDAAAPGDE	PAPPAALPSP	AKRPRETPSH	ADPPGGASKP	KKULIVSELAE	-1111
	HSV1-Patton		PAPPAALPSP			RKLLVSELAE	
20	HSV1-DJL	ELDAAAPGDE	PAPPAALPSP	AKRPRETPSP	ADPPGGASKP		
30	HSV1-F	ELDAAAPGDE	PAPPAALPSP	AKRPRETPLH	ADPPGGASKP	KVDDADENVE	
	********	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	DE MUNICIPALITA	TTONNOTUMEN	ALFGNNAKIT	FCT.T.VDFTDF	_1197
	HSV2-MS	DPGYALARGV	PLNTDYYFSH	LLGAACVIFK	ALFGNNAKIT	ECTINDELDE	_1100
	HSV2-186	DPGYATARGV	PLNTDYYFSH	LLGAACVIFK	ALFGNNAKIT	FOURTAINETER	_119/
~ ~	HSV-Kos	DPAYALAHGV	ALNTDYYFSH	LLGAACVIFK	ALFGNNAKIT	FOUNDATION	-1104
35	HSV1-Patton	DPAYALAHGV	ALNTDYYFSH	LLGAACVITK	ALFGNNAKIT	ECLIADALDE ESPUKKLTER	-1194
	HSV1-DJL	DPAYALAHGV	ALNTDYYFSH	LLGAACVITK	ALEGNMANT1	ESTITUTE TER	-1194
	HSV1-F	DPAYAIAHGV	ALNTDYYFSH	LLGAACVTFK	ALFGNNAKIT	FOURTKETEE	-1194
			DI DA 3 CECDA		DMT TID A DINIT	n ★ _102Q	
	HSV2-MS	TWHPPDDVAA	RLRAAGFGPA	GAGATAEETR	RMLHRAFDTL	A" -1230	
40	HSV2-186	TWHPPDDVAA	RLRAAGFGPA	GAGATAEETR	RMLHRAFDTL	A" -124U	
	HSV-Kos	VWHPPDDVAA	RLRAAGFGAV	GAGATAEETR	RMLHRAFDTL	WT722	
	HSV1-Patton	VWHPPDDVTA	RLRAAGFGAV	GAGATAEETR	RMLHRAFDTL	A~ -1235	
	HSV1-DJL	VWHPPDDVAA	RLRTAGFGAV	GAGATAEETR	RMLHRAFDTL	A^ -1235	
	HSV1-F	VWHPPDDVAA	. RLRAAGFGAV	GAGATAEETR	RMLHRAFDTL	A~ -1235	
45							

<sup>\*</sup>Amino acid alignment demonstrates difference in amino acid's sequences.

<sup>\*</sup>The gaps "...." indicate missing amino acids relative to other stanins.

<sup>\*</sup>Wild HSV2-MS is listed as SEQ. ID NO 14.

<sup>\*</sup>Wild HSV2-186 is listed as SEQ. ID NO 15.

<sup>\*</sup>Wild HSV-Kos is listed as SEQ. ID NO 16.

<sup>\*</sup>Wild HSV1-Patton is listed as SEQ. ID NO 17.

<sup>\*</sup>Wild HSV1-DJL is listed as SEQ. ID NO 18.

<sup>\*</sup>Wild HSV1-F is listed as SEQ. ID NO 19.

### Figure 5 DNA and amino acid sequence list

SEQ. ID. NO. 1 DNA sequence of DNA polymerase gene for HSV2-MS-M1 1 ATGTTTTGTG CCGCGGCGG CCCGACTTCC CCCGGGGGGA AGTCGGCGGC 5 51 TCGGGCGGCG TCTGGGTTTT TTGCCCCCCA CAACCCCCGG GGAGCCACCC 101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCACCTC 10 151 GCTCAGACCG GAACGCAGCC AAAGGCCCCC GGGCCGGCTC AGCGCCATAC 201 GTACTACAGC GAGTGCGACG AATTTCGATT TATCGCCCCG CGTTCGCTGG 251 ACGAGGACGC CCCCGCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC 15 301 CGGCGCGCC CTAAGGTGTA CTGCGGGGGG GACGAGCGCG ACGTCCTCCG 351 CGTGGGCCCG GAGGGCTTCT GGCCGCGTCG CTTGCGCCTG TGGGGCGGTG 20 401 CGGACCATGC CCCCAAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG 451 TACGACATCC TGGAGCACGT GGAACACGCG TACAGCATGC GCGCCGCCCA 501 GCTCCACGAG CGATTTATGG ACGCCATCAC GCCCGCCGGG ACCGTCATCA 25 551 CGCTTCTGGG TCTGACCCCC GAAGGCCATC GCGTCGCCGT TCACGTCTAC 601 GGCACGCGGC AGTACTTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT 30 651 GCAGTGCCGT GCCCGCGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC 701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGCA TCTCCGCGGA CCACTTCGAG 751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC 35 801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG GCGCGCGCTG GCCTACCTGT 851 GCGACAACTT TTGCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC 40 901 ACCACCGGT TTATCCTGGA CAACCCGGGG TTTGTCACCT TCGGCTGGTA 951 CCGCCTCAAG CCCGGCCGCG GGAACGCGCC GGCCCAACCG CGCCCCCGA 1001 CGGCGTTCGG AACCTCGAGC GACGTCGAGT TTAACTGCAC GGCGGACAAC 45 1051 CTGGCCGTCG AGGGGGCCAT GTGTGACCTG CCGGCCTACA AGCTCATGTG 1101 CTTCGATATC GAATGCAAGG CCGGGGGGGA GGACGAGCTG GCCTTTCCGG 50 1151 TCGCGGAACG CCCGGAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC 1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCCTGTTTT CGCTCGGATC 1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCCTCC AGGGGCCTGC 55 1301 CGGCCCCGT CGTCCTGGAG TTTGACAGCG AATTCGAGAT GCTGCTGGCC

	1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTTCGTGA CCGGGTACAA
	1401 CATCATCAAC TTCGACTGGC CCTTCGTCCT GACCAAGCTG ACGGAGATCT
5	1451 ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTTC
	1501 CGCGTGTGGG ACATCGGCCA GAGCCACTTT CAGAAGCGCA GCAAGATCAA
10	1551 GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG
10	1601 TCAAACTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG
	1651 GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCCT ACTACGCCTC
15	1701 CGGGCCCGCG CAGCGCGGGG TGATCGGCGA GTATTGTGTG CAGGACTCGC
	1751 TGCTGGTCGG GCAGCTGTTC TTCAAGTTTC TGCCGCACCT GGAGCTTTCC
20	1801 GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG
20	1851 CCAGCAGATC CGCGTCTTCA CGTGCCTCCT GCGCCTTGCG GGCCAGAAGG
	1901 GCTTCATCCT GCCGGACACC CAGGGGCGGT TTCGGGGCCT CGACAAGGAG
25	1951 GCGCCCAAGC GCCCGGCCGT GCCTCGGGGG GAAGGGGAGC GGCCGGGGGA
	2001 CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGAG GACGGGGACG
30	2051 AGCGCGAGGA GGTCGCGCGC GAGACCGGGG GCCGGCACGT TGGGTACCAG
30	2101 GGGGCCCGGG TCCTCGACCC CACCTCCGGG TTTCACGTCG ACCCCGTGGT
	2151 GGTGTTTGAC TTTGCCAGCC TGTACCCCAG CATCATCCAG GCCCACAACC
35	2201 TGTGCTTCAG TACGCTCTCC CTGCGGCCCG AGGCCGTCGC GCACCTGGAG
	2251 GCGGACCGGG ACTACCTGGA GATCGAGGTG GGGGGCCGAC GGCTGTTCTT
40	2301 CGTGAAGGCC CACGTACGCG AGAGCCTGCT GAGCATCCTG CTGCGCGACT
40	2351 GGCTGGCCAT GCGAAAGCAG ATCCGCTCGC GGATCCCCCA GAGCACCCCC
	2401 GAGGAGGCCG TCCTCCTCGA CAAGCAACAG GCCGCCATCA AGGTGGTGTG
45	2451 CAACTCGGTG TACGGGTTCA CCGGGGCGCA GCACGGTCTT CTGCCCTGCC
	2501 TGCACGTGGC CGCCACCGTG ACGACCATCG GCCGCGAGAT GCTCCTCGCG
50	2551 ACGCGCGCGT ACGTGCACGC GCGCTGGGCG GAGTTCGATC AGCTGCTGGC
30	2601 CGACTTTCCG GAGGCGGCCG GCATGCGCGC CCCCGGTCCG TACTCCATGC
	2651 GCATCATCTA CGGGGACACG GACTCCATTT TCGTTTTGTG CCGCGGCCTC
55	2701 ACGGCCGCGG GCCTGGTGGC CATGGGCGAC AAGATGGCGA GCCACATCTC
	2751 GCGCGCGCTG TTCCTCCCCC CGATCAAGCT CGAGTGCGAA AAAACGTTCA
60	2801 CCAAGCTGCT GCTCATCGCC AAGAAAAAGT ACATCGGCGT CATCTGCGGG

	2851 GGCAAGATGC TCATCAAGGG CGTGGATCTG GTGCGCAAAA ACAACTGCGC
	2901 GTTTATCAAC CGCACCTCCA GGGCCCTGGT CGACCTGCTG TTTTACGACG
5	2951 ATACCGTATC CGGAGCGCC GCCGCGTTAG CCGAGCGCCC CGCAGAGGAG
	3001 TGGCTGGCGC GACCCCTGCC CGAGGGACTG CAGGCGTTCG GGGCCGTCCT
10	3051 CGTAGACGCC CATCGGCGCA TCACCGACCC GGAGAGGGAC ATCCAGGACT
10	3101 TTGTCCTCAC CGCCGAACTG AGCAGACACC CGCGCGCGTA CACCAACAAG
	3151 CGCCTGGCCC ACCTGACGGT GTATTACAAG CTCATGGCCC GCCGCGCGCA
15	3201 GGTCCCGTCC ATCAAGGACC GGATCCCGTA CGTGATCGTG GCCCAGACCC
	3251 GCGAGGTAGA GGAGACGGTC GCGCGGCTGG CCGCCCTCCG CGAGCTAGAC
20	3301 GCCGCCGCCC CAGGGGACGA GCCCGCCCCC CCAGCGGCCC TGCCCTCCCC
20	3351 GGCCAAGCGC CCCCGGGAGA CGCCGTCGCA TGCCGACCCC CCGGGAGGCG
	3401 CGTCCAAGCC CCGCAAGCTG CTGGTGTCCG AGCTGGCGGA GGATCCCGGG
25	3451 TACGCCATCG CCCGGGGCGT TCCGCTCAAC ACGGACTATT ACTTCTCGCA
	3501 CCTGCTGGGG GCGGCCTGCG TGACGTTCAA GGCCCTGTTT GGAAATAACG
20	3551 CCAAGATCAC CGAGAGTCTG TTAAAGAGGT TTATTCCCGA GACGTGGCAC
30	3601 CCCCCGGACG ACGTGGCCGC GCGGCTCAGG GCCGCGGGGT TCGGGCCGGC
	3651 GGGGGCCGGC GCTACGGCGG AGGAAACTCG TCGAATGTTG CATAGAGCCT
35	3701 TTGATACTCT AGCATGA

SEQ. ID. NO. 2 Amino acid sequence of DNA polymerase for HSV2-MS-M1

1 MFCAAGGPTS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL 51 AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL 5 101 RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPKG FDPTVTVFHV 151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY 10 201 GTRQYFYMNK AEVDRHLQCR APRDLCERLA AALRESPGAS FRGISADHFE 251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA 301 TTRFILDNPG FVTFGWYRLK PGRGNAPAQP RPPTAFGTSS DVEFNCTADN 15 351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY 401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA 20 451 FMTFVKQYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF 501 RVWDIGQSHF.QKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK 551 DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS 25 601 AVARLAGINI TRTIYDGQQI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE 651 APKRPAVPRG EGERPGDGNG DEDKDDDEDE DGDEREEVAR ETGGRHVGYQ 30 701 GARVLDPTSG FHVDPVVVFD FASLYPSIIQ AHNLCFSTLS LRPEAVAHLE 751 ADRDYLEIEV GGRRLFFVKA HVRESLLSIL LRDWLAMRKQ IRSRIPQSTP 801 EEAVLLDKQQ AAIKVVCNSV YGFTGAQHGL LPCLHVAATV TTIGREMLLA 35 851 TRAYVHARWA EFDQLLADFP EAAGMRAPGP YSMRIIYGDT DSIFVLCRGL 901 TAAGLVAMGD KMASHISRAL FLPPIKLECE KTFTKLLLIA KKKYIGVICG 40 951 GKMLIKGVDL VRKNNCAFIN RTSRALVDLL FYDDTVSGAA AALAERPAEE 1001 WLARPLPEGL QAFGAVLVDA HRRITDPERD IQDFVLTAEL SRHPRAYTNK 1051 RLAHLTVYYK LMARRAQVPS IKDRIPYVIV AQTREVEETV ARLAALRELD 45 1101 AAAPGDEPAP PAALPSPAKR PRETPSHADP PGGASKPRKL LVSELAEDPG 1151 YAIARGVPLN TDYYFSHLLG AACVTFKALF GNNAKITESL LKRFIPETWH 50 1201 PPDDVAARLR AAGFGPAGAG ATAEETRRML HRAFDTLA\*

SEQ.ID.NO. 3 DNA sequence of DNA polymerase gene for HSV2-186-M1

1 ATGTTTTGTG CCGCGGCGG CCCGGCTTCC CCCGGGGGA AGTCGGCGGC 51 TCGGGCGCG TCTGGGTTTT TTGCCCCCCA CAACCCCCGG GGAGCCACCC 5 101 AGACGGCACC GCCGCCTTGC CGCCGGCAGA ACTTCTACAA CCCCCACCTC 151 GCTCAGACCG GAACGCAGCC AAAGGCCCCC GGGCCGGCTC AGCGCCATAC 10 201 GTACTACAGC GAGTGCGACG AATTTCGATT TATCGCCCCG CGTTCGCTGG 251 ACGAGGACGC CCCCGCGGAG CAGCGCACCG GGGTCCACGA CGGCCGCCTC 301 CGGCGCCCC CTAAGGTGTA CTGCGGGGGG GACGAGCGCG ACGTCCTCCG 15 351 CGTGGGCCCG GAGGGCTTCT GGCCGCGTCG CTTGCGCCTG TGGGGCGGTG 401 CGGACCATGC CCCCGAGGGG TTCGACCCCA CCGTCACCGT CTTCCACGTG 20 451 TACGACATCC TGGAGCACGT GGAACACGCG TACAGCATGC GCGCCGCCCA 501 GCTCCACGAG CGATTTATGG ACGCCATCAC GCCCGCCGGG ACCGTCATCA 551 CGCTTCTGGG TCTGACCCCC GAAGGCCATC GCGTCGCCGT TCACGTCTAC 25 601 GGCACGCGGC AGTACTTTTA CATGAACAAG GCGGAGGTGG ATCGGCACCT 651 GCAGTGCCGT GCCCCGCGCG ATCTCTGCGA GCGCCTGGCG GCGGCCCTGC 30 701 GCGAGTCGCC GGGGGCGTCG TTCCGCGGCA TCTCCGCGGA CCACTTCGAG 751 GCGGAGGTGG TGGAGCGCGC CGACGTGTAC TATTACGAAA CGCGCCCGAC 801 CCTGTACTAC CGCGTCTTCG TGCGAAGCGG GCGCGCGCTG GCCTACCTGT 35 851 GCGACAACTT TTGCCCCGCG ATCAGGAAGT ACGAGGGGGG CGTCGACGCC 901 ACCACCGGT TTATCCTGGA CAACCGGGG TTTGTCACCT TCGGCTGGTA 40 951 CCGCCTCAAG CCCGGCCGCG GGAACGCGCC GGCCCAACCG CGCCCCCCGA 1001 CGGCGTTCGG AACCTCGAGC GACGTCGAGT TTAACTGCAC GGCGGACAAC 1051 CTGGCCGTCG AGGGGGCCAT GTGTGACCTG CCGGCCTACA AGCTCATGTG 45 1101 CTTCGATATC GAATGCAAGG CCGGGGGGGA GGACGAGCTG GCCTTTCCGG 1151 TCGCGGAACG CCCGGAAGAC CTCGTCATCC AGATCTCCTG TCTGCTCTAC 50 1201 GACCTGTCCA CCACCGCCCT CGAGCACATC CTCCTGTTTT CGCTCGGATC 1251 CTGCGACCTC CCCGAGTCCC ACCTCAGCGA TCTCGCCTCC AGGGGCCTGC 1301 CGGCCCCGT CGTCCTGGAG TTTGACAGCG AATTCGAGAT GCTGCTGGCC 55 1351 TTCATGACCT TCGTCAAGCA GTACGGCCCC GAGTTCGTGA CCGGGTACAA 1401 CATCATCAAC TTCGACTGGC CCTTCGTCCT GACCAAGCTG ACGGAGATCT 60

	1451	ACAAGGTCCC GCTCGACGGG TACGGGCGCA TGAACGGCCG GGGTGTGTTC
	1501	CGCGTGTGGG ACATCGGCCA GAGCCACTTT CAGAAGCGCA GCAAGATCAA
5	1551	GGTGAACGGG ATGGTGAACA TCGACATGTA CGGCATCATC ACCGACAAGG
	1601	TCAAACTCTC CAGCTACAAG CTGAACGCCG TCGCCGAGGC CGTCTTGAAG
10	1651	GACAAGAAGA AGGATCTGAG CTACCGCGAC ATCCCCGCCT ACTACGCCTC
10	1701	CGGGCCCGCG CAGCGCGGGG TGATCGGCGA GTATTGTGTG CAGGACTCGC
	1751	TGCTGGTCGG GCAGCTGTTC TTCAAGTTTC TGCCGCACCT GGAGCTTTCC
15	1801	GCCGTCGCGC GCCTGGCGGG CATCAACATC ACCCGCACCA TCTACGACGG
	1851	CCAGCAGATC CGCGTCTTCA CGTGCCTCCT GCGCCTTGCG GGCCAGAAGG
20	1901	GCTTCATCCT GCCGGACACC CAGGGGCGGT TTCGGGGCCT CGACAAGGAG
20	1951	GCGCCCAAGC GCCCGGCCGT GCCTCGGGGG GAAGGGGAGC GGCCGGGGGA
	2001	CGGGAACGGG GACGAGGATA AGGACGACGA CGAGGACGG GACGAGGACG
25	2051	GGGACGAGCG CGAGGAGGTC GCGCGCGAGA CCGGGGGCCG GCACGTTGGG
	2101	TACCAGGGGG CCCGGGTCCT CGACCCCACC TCCGGGTTTC ACGTCGACCC
30	2151	CGTGGTGGTG TTTGACTTTG CCAGCCTGTA CCCCAGCATC ATCCAGGCCC
50	2201	ACAACCTGTG CTTCAGTACG CTCTCCCTGC GGCCCGAGGC CGTCGCGCAC
_	2251	CTGGAGGCGG ACCGGGACTA CCTGGAGATC GAGGTGGGGG GCCGACGGCT
35	2301	GTTCTTCGTG AAGGCCCACG TACGCGAGAG CCTGCTGAGC ATCCTGCTGC
	2351	GCGACTGGCT GGCCATGCGA AAGCAGATCC GCTCGCGGAT CCCCCAGAGC
40	2401	CCCCCGAGG AGGCCGTCCT CCTCGACAAG CAACAGGCCG CCATCAAGGT
40	2451	GGTGTGCAAC TCGGTGTACG GGTTCACCGG GGCGCAGCAC GGTCTTCTGC
	2501	CCTGCCTGCA CGTGGCCGCC ACCGTGACGA CCATCGGCCG CGAGATGCTC
45	2551	CTCGCGACGC GCGCGTACGT GCACGCGCGC TGGGCGGAGT TCGATCAGCT
	2601	GCTGGCCGAC TTTCCGGAGG CGGCCGGCAT GCGCGCCCCC GGTCCGTACT
50	2651	CCATGCGCAT CATCTACGGG GACACGGACT CCATTTTCGT TTTGTGCCGC
30	2701	GGCCTCACGG CCGCGGGCCT GGTGGCCATG GGCGACAAGA TGGCGAGCCA
	2751	CATCTCGCGC GCGCTGTTCC TCCCCCCGAT CAAGCTCGAG TGCGAAAAAA
55	2801	CGTTCACCAA GCTGCTGCTC ATCGCCAAGA AAAAGTACAT CGGCGTCATC
	2851	TGCGGGGGCA AGATGCTCAT CAAGGGCGTG GATCTGGTGC GCAAAAACAA
60	2901	CTGCGCGTTT ATCAACCGCA CCTCCAGGGC CCTGGTCGAC CTGCTGTTTT
50		

	2951 ACGACGATAC CGTATCCGGA GCGCCCGCG CGTTAGCCGA GCGCCCCGCA
	3001 GAGGAGTGGC TGGCGCGACC CCTGCCCGAG GGACTGCAGG CGTTCGGGGC
5	3051 CGTCCTCGTA GACGCCCATC GGCGCATCAC CGACCCGGAG AGGGACATCC
	3101 AGGACTTTGT CCTCACCGCC GAACTGAGCA GACACCCGCG CGCGTACACC
10	3151 AACAAGCGCC TGGCCCACCT GACGGTGTAT TACAAGCTCA TGGCCCGCCG
10	3201 CGCGCAGGTC CCGTCCATCA AGGACCGGAT CCCGTACGTG ATCGTGGCCC
	3251 AGACCCGCGA GGTAGAGGAG ACGGTCGCGC GGCTGGCCGC CCTCCGCGAG
15	3301 CTAGACGCCG CCGCCCCAGG GGACGAGCCC GCCCCCCAG CGGCCCTGCC
	3351 CTCCCCGGCC AAGCGCCCCC GGGAGACGCC GTCGCATGCC GACCCCCCGG
20	3401 GAGGCGCGTC CAAGCCCCGC AAGCTGCTGG TGTCCGAGCT GGCGGAGGAT
20	3451 CCCGGGTACG CCATCGCCCG GGGCGTTCCG CTCAACACGG ACTATTACTT
	3501 CTCGCACCTG CTGGGGGCGG CCTGCGTGAC GTTCAAGGCC CTGTTTGGAA
25	3551 ATAACGCCAA GATCACCGAG AGTCTGTTAA AGAGGTTTAT TCCCGAGACG
	3601 TGGCACCCCC CGGACGACGT GGCCGCGCGC CTCAGGGCCG CGGGGTTCGG
30	3651 GCCGGCGGGGGCGCTA CGGCGGAGGA AACTCGTCGA ATGTTGCATA
50	3701 GAGCCTTTGA TACTCTAGCA TGA

SEQ.ID.NO. 4 Amino acid sequence of DNA polymerase for HSV2-186-M1 5 1 MFCAAGGPAS PGGKSAARAA SGFFAPHNPR GATQTAPPPC RRQNFYNPHL 51 AQTGTQPKAP GPAQRHTYYS ECDEFRFIAP RSLDEDAPAE QRTGVHDGRL 101 RRAPKVYCGG DERDVLRVGP EGFWPRRLRL WGGADHAPEG FDPTVTVFHV 10 151 YDILEHVEHA YSMRAAQLHE RFMDAITPAG TVITLLGLTP EGHRVAVHVY 201 GTROYFYMNK AEVDRHLOCR APROLCERLA AALRESPGAS FRGISADHFE 15 251 AEVVERADVY YYETRPTLYY RVFVRSGRAL AYLCDNFCPA IRKYEGGVDA 301 TTRFILDNPG FVTFGWYRLK PGRGNAPAOP RPPTAFGTSS DVEFNCTADN 351 LAVEGAMCDL PAYKLMCFDI ECKAGGEDEL AFPVAERPED LVIQISCLLY 20 401 DLSTTALEHI LLFSLGSCDL PESHLSDLAS RGLPAPVVLE FDSEFEMLLA 451 FMTFVKOYGP EFVTGYNIIN FDWPFVLTKL TEIYKVPLDG YGRMNGRGVF 501 RVWDIGOSHF OKRSKIKVNG MVNIDMYGII TDKVKLSSYK LNAVAEAVLK 25 551 DKKKDLSYRD IPAYYASGPA QRGVIGEYCV QDSLLVGQLF FKFLPHLELS 601 AVARLAGINI TRTIYDGOOI RVFTCLLRLA GQKGFILPDT QGRFRGLDKE 30 651 APKRPAVPRG EGERPGDGNG DEDKDDDEDG DEDGDEREEV ARETGGRHVG 701 YQGARVLDPT SGFHVDPVVV FDFASLYPSI IQAHNLCFST LSLRPEAVAH 35 751 LEADRDYLEI EVGGRRLFFV KAHVRESLLS ILLRDWLAMR KQIRSRIPQS 801 PPEEAVLLDK OOAAIKVVCN SVYGFTGAOH GLLPCLHVAA TVTTIGREML 851 LATRAYVHAR WAEFDOLLAD FPEAAGMRAP GPYSMRIIYG DTDSIFVLCR 40 901 GLTAAGLVAM GDKMASHISR ALFLPPIKLE CEKTFTKLLL IAKKKYIGVI 951 CGGKMLIKGV DLVRKNNCAF INRTSRALVD LLFYDDTVSG AAAALAERPA 1001 EEWLARPLPE GLOAFGAVLV DAHRRITDPE RDIQDFVLTA ELSRHPRAYT 45 1051 NKRLAHLTVY YKLMARRAQV PSIKDRIPYV IVAQTREVEE TVARLAALRE 1101 LDAAAPGDEP APPAALPSPA KRPRETPSHA DPPGGASKPR KLLVSELAED 50 1151 PGYAIARGVP LNTDYYFSHL LGAACVTFKA LFGNNAKITE SLLKRFIPET 1201 WHPPDDVAAR LRAAGFGPAG AGATAEETRR MLHRAFDTLA \*

SEQ.ID.NO. 5

DNA sequence of DNA polymerase gene for HSV1-KOS-M1

1 ATGTTTTCCG GTGGCGGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC 5 51 CAGGGCGGCG TCCGGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC 101 GGGGACCCC GCCTTGTTTG AGGCAAAACT TTTACAACCC CTACCTCGCC 151 CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA 10 201 CTATAGCGAA TGCGATGAAT TTCGATTCAT CGCCCCGCGG GTGCTGGACG 251 AGGATGCCCC CCCGGAGAAG CGCGCCGGGG TGCACGACGG TCACCTCAAG 15 301 CGCGCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT 351 CGGGTCGGGC GGCTTCTGGC CGCGCGCTC GCGCCTGTGG GGCGGCGTGG 401 ACCACGCCC GGCGGGGTTC AACCCCACCG TCACCGTCTT TCACGTGTAC 20 451 GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCAGTT 501 CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC 25 551 TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC 601 ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTTGACA GGCACCTACA 651 ATGCCGCGCC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG 30 701 AGTCCCGGG CGCGTCGTTC CGCGGCATCT CCGCGGACCA CTTCGAGGCG 751 GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCGCTCT 801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTCG TACCTGTGCG 35 851 ACAACTTCTG CCCGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC 901 ACCCGGTTCA TCCTGGACAA CCCCGGGTTC GTCACCTTCG GCTGGTACCG 40 951 TCTCAAACCG GGCCGGAACA ACACGCTAGC CCAGCCGCGG GCCCCGATGG 1001 CCTTCGGGAC ATCCAGCGAC GTCGAGTTTA ACTGTACGGC GGACAACCTG 1051 GCCATCGAGG GGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT 45 1101 CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG 1151 CCGGGCACCC GGAGGACCTG GTTATTCAGA TATCCTGTCT GCTCTACGAC 50 1201 CTGTCCACCA CCGCCCTGGA GCACGTCCTC CTGTTTTCGC TCGGTTCCTG 1251 CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCCA 55 1301 CGCCCGTGGT TCTGGAATTC GACAGCGAAT TCGAGATGCT GTTGGCCTTC 1351 ATGACCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT 1401 CATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGTTGACG GACATTTACA 60

	1451	AGGTCCCCCT GGACGGGTAC GGCCGCATGA ACGGCCGGGG CGTGTTTCGC
	1501	GTGTGGGACA TAGGCCAGAG CCACTTCCAG AAGCGCAGCA AGATAAAGGT
5	1551	GAACGGCATG GTGAACATCG ACATGTACGG GATCATAACC GACAAGATCA
	1601	AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC
10	1651	AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCGCCTACT ACGCCGCCGG
10	1701	GCCCGCGCAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC
	1751	TGGTGGGCCA GCTGTTTTTT AAGTTTTTGC CCCATCTGGA GCTCTCGGCC
15	1801	GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA
	1851	GCAGATCCGC GTCTTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT
20	1901	TTATTCTGCC GGACACCCAG GGGCGATTTA GGGGCGCCGG GGGGAGGCG
20	1951	CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA
	2001	GGGGGAGGAC GAGGACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG
25	2051	AGGGCGCGC GGAGACCGCC GGCCGGCACG TGGGGTACCA GGGGGCCAGG
	2101	GTCCTTGACC CCACTTCCGG GTTTCACGTG AACCCCGTGG TGGTGTTCGA
30	2151	CTTTGCCAGC CTGTACCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA
30	2201	GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGCAAG
	2251	GACTACCTGG AGATCGAGGT GGGGGGGGCGA CGGCTGTTCT TCGTCAAGGC
35	2301	TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA
	2351	TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC
40	2401	GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT
40	2451	GTACGGGTTC ACGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG
	2501	CCGCGACGGT GACGACCATC GGCCGCGAGA TGCTGCTCGC GACCCGCGAG
45	2551	TACGTCCACG CGCGCTGGGC GGCCTTCGAA CAGCTCCTGG CCGATTTCCC
	2601	GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT
50	2651	ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC
30	2701	GGGCTGACGG CCATGGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT
	2751	GTTTCTGCCC CCCATCAAAC TCGAGTGCGA AAAGACGTTC ACCAAGCTGC
55	2801	TGCTGATCGC CAAGAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG
	2851	CTCATCAAGG GCGTGGATCT GGTGCGCAAA AACAACTGCG CGTTTATCAA
60	2901	CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATACCGTAT
~~		

		2951 CCGGAGCGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG
		3001 CGACCCCTGC CCGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC
	5	3051 CCATCGGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTCCTCA
		3101 CCGCCGAACT GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC
	10	3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC
	10	3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG
		3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC
	15 .	3301 CCAGGGGACG AGCCCGCCCC CCCCGCGGCC CTGCCCTCCC CGGCCAAGCG
		3351 CCCCCGGGAG ACGCCGTCGC ATGCCGACCC CCCGGGAGGC GCGTCCAAGC
20	20	3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT
	20	3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG
		3501 GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA
	25	3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC
		3601 GACGTGGCCG CGCGGCTCCG GGCCGCAGGG TTCGGGGCGG TGGGTGCCGG
20	30	3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC
	50	3701 TAGCATGA

Amino acid sequence of DNA polymerase for HSV1-KOS-M1 SEO.ID.NO. 6 1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA 5 51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY 10 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG 201 TROYFYMNKE EVDRHLOCRA PROLCERMAA ALRESPGASF RGISADHFEA 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT 15 301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF 20 451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR 501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD 25 551 KKKDLSYRDI PAYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA 601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGAGGEA 30 651 PKRPAAARED EERPEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR 701 VLDPTSGFHV NPVVVFDFAS LYPSIIOAHN LCFSTLSLRA DAVAHLEAGK 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA 35 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE 851 YVHARWAAFE OLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA 901 GLTAMGDKMA SHISRALFLP PIKLECEKTF TKLLLIAKKK YIGVIYGGKM 40 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA 1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA 45 1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA 1101 PGDEPAPPAA LPSPAKRPRE TPSHADPPGG ASKPRKLLVS ELAEDPAYAI 1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD 50 1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA\*

## SEQ.ID.NO. 7 DNA sequence of HSV polymerase gene for HSV1-F-M1

5	1	ATGTTTTCCG	GTGGCGGCGG	CCCGCTGTCC	CCCGGAGGAA	AGTCGGCGGC
3	51	CAGGGCGGCG	TCCGGGTTTT	TTGCGCCCGC	CGGCCCTCGC	GGAGCCGGCC
	101	GGGGACCCCC	GCCTTGCTTG	AGGCAAAACT	TTTACAACCC	CTACCTCGCC
10	151	CCAGTCGGGA	CGCAACAGAA	GCCGACCGGG	CCAACCCAGC	GCCATACGTA
	201	CTATAGCGAA	TGCGATGAAT	TTCGATTCAT	CGCCCCGCGG	GTGCTGGACG
1.5	251	AGGATGCCCC	CCCGGAGAAG	CGCGCCGGGG	TGCACGACGG	TCACCTCAAG
15	301	CGCGCCCCA	AGGTGTACTG	CGGGGGGGAC	GAGCGCGACG	TCCTCCGCGT
	351	CGGGTCGGGC	GGCTTCTGGC	CGCGGCGCTC	GCGCCTGTGG	GGCGGCGTGG
20	401	ACCACGCCCC	GGCGGGGTTC	AACCCCACCG	TCACCGTCTT	TCACGTGTAC
	451	GACATCCTGG	AGAACGTGGA	GCACGCGTAC	GGCATGCGCG	CGGCCCAGTT
25	501	CCACGCGCGG	TTTATGGACG	CCATCACACC	GACGGGGACC	GTCATCACGC
23	551	TCCTGGGCCT	GACTCCGGAA	GGCCACCGGG	TGGCCGTTCA	CGTTTACGGC
•	601	ACGCGGCAGT	ACTTTTACAT	GAACAAGGAG	GAGGTCGACA	GGCACCTACA
30	651	ATGCCGCGCC	CCACGAGATC	TCTGCGAGCG	CATGGCCGCG	GCCCTGCGCG
	701	AGTCCCCGGG	CGCGTCGTTC	CGCGGCATTT	CCGCGGACCA	CTTCGAGGCG
35	751	GAGGTGGTGG	AGCGCACCGA	CGTGTACTAC	TACGAGACGC	GCCCCGCTCT
33	801	GTTTTACCGC	GTCTACGTCC	GAAGCGGGCG	CGTGCTGTCG	TACCTGTGCG
	851	ACAACTTCTG	CCCGGCCATC	AAGAAGTACG	AGGGTGGGGT	CGACGCCACC
40	901	ACCCGGTTCA	TCCTGGACAA	CCCCGGGTTC	GTCACCTTCG	GCTGGTACCG
	951	TCTCAAACCG	GGCCGGAACA	ACACGCTAGC	CCAGCCGCGG	GCCCCGATGG
45	1001	CCTTCGGGAC	ATCCAGCGAC	GTCGAGTTTA	ACTGTACGGC	GGACAACCTG
43	1051	GCCATCGAGG	GGGGCATGAG	CGACCTACCG	GCATACAAGC	TCATGTGCTT
	1101	CGATATCGAA	TGCAAGGCGG	GGGGGGAGGA	CGAGCTGGCC	TTTCCGGTGG
50	1151	CCGGGCACCC	GGAGGACCTG	GTCATCCAGA	TATCCTGTCT	GCTCTACGAC
	1201	CTGTCCACCA	CCGCCCTGG	GCACGTCCTC	CTGTTTTCGC	TCGGTTCCTG
55	1251	CGACCTCCCC	GAATCCCACC	TGAACGAGCT	GGCGGCCAGG	GGCCTGCCCA
33	1301	CGCCCGTGGT	TCTGGAATTC	GACAGCGAAT	TCGAGATGCT	GTTGGCCTTC
	1351	ATGACCCTTG	TGAAACAGT	A CGGCCCCGAG	TTCGTGACCG	GGTACAACAT
60	1401	CATCAACTTC	GACTGGCCCT	TCTTGCTGGC	CAAGCTGACG	GACATTTACA
	1451	AGGTCCCCCT	GGACGGGTA	GGCCGCATGA	. ACGGCCGGGG	CGTGTTTCGC
65	1501	GTGTGGGAC	A TAGGCCAGAG	G CCACTTCCAG	AAGCGCAGCA	AGATAAAGGT
05	1551	GAACGGCATC	GTGAACATC	3 ACATGTACGG	GATTATAACC	GACAAGATCA

	1601	AGCTCTCGAG	CTACAAGCTC	AACGCCGTGG	CCGAAGCCGT	CCTGAAGGAC
~	1651	AAGAAGAAGG	ACCTGAGCTA	TCGCGACATC	CCCGCCTACT	ACGCCGCCGG
5	1701	GCCCGCGCAA	CGCGGGGTGA	TCGGCGAGTA	CTGCATACAG	GATTCCCTGC
	1751	TGGTGGGCCA	GCTGTTTTT	AAGTTTTTGC	CCCATCTGGA	GCTCTCGGCC
10	1801	GTCGCGCGCT	TGGCGGGTAT	TAACATCACC	CGCACCATCT	ACGACGGCCA
	1851	GCAGATCCGC	GTCTTTACGT	GCCTGCTGCG	CCTGGCCGAC	CAGAAGGGCT
1.5	1901	${\tt TTATTCTGCC}$	GGACACCCAG	GGGCGATTTA	GGGGCGGCGG	GGGGGAGGCG
15	1951	CCCAAGCGTC	CGGCCGCAGC	CCGGGAGGAC	GAGGAGCGGC	CAGAGGAGGA
	2001	GGGGGAGGAC	GAGGACGAAC	GCGAGGAGGG	CGGGGGCGAG	CGGGAGCCGG
20	2051	AGGGCGCGCG	GGAGACCGCC	GGCCGGCACG	TGGGGTACCA	GGGGGCCAGG
	2101	GTCCTTGACC	CCACTTCCGG	GTTTCATGTG	AACCCCGTGG	TGGTGTTCGA
05	2151	CTTTGCCAGC	CTGTACCCCA	GCATCATCCA	GGCCCACAAC	CTGTGCTTCA
25	2201	GCACGCTCTC	CCTGAGGGCC	GACGCAGTGG	CGCACCTGGA	GGCGGGÇAAG
	2251	GACTACCTGG	AGATCGAGGT	GGGGGGGCGA	CGGCTGTTCT	TCGTCAAGGC
30	2301	TCACGTGCGA	GAGAGCCTCC	TCAGCATCCT	CCTGCGGGAC	TGGCTCGCCA
	2351	TGCGAAAGCA	GATCCGCTCG	CGGATTCCCC	AGAGCAGCCC	CGAGGAGGCC
25	2401	GTGCTCCTGG	ACAAGCAGCA	GGCCGCCATC	AAGGTCGTGT	GTAACTCGGT
35	2451	TTACGGGTTC	ACGGGAGCGC	AGCACGGACT	CCTGCCGTGC	CTGCACGTTG
	2501	CCGCGACGGT	GACGACCATC	GGCCGCGAGA	TGCTGCTCGC	GACCCGCGAG
40	2551	TACGTCCACG	CGCGCTGGGC	GGCCTTCGAA	CAGCTCCTGG	CCGATTTCCC
	2601	GGAGGCGGCC	GACATGCGCG	CCCCGGGCC	CTATTCCATG	CGCATCATCT
45	2651	ACGGGGACAC	GGACTCCATC	TTTGTGCTGT	GCCGCGGCCT	CACGGCCGCC
45	2701	GGGCTGACGG	CCGTGGGCGA	CAAGATGGCG	AGCCACATCT	CGCGCGCGCT
	2751	GTTTCTGTCC	CCCATCAAAC	TCGAGTGCGA	AAAGACGTTC	ACCAAGCTGC
50	2801	TGCTGATCGC	CAAGAAAAAG	TACATCGGCG	TCATCTACGG	GGGTAAGATG
	2851	CTCATCAAGG	GCGTGGATCT	GGTGCGCAAA	AACAACTGCG	CGTTTATCAA
55	2901	CCGCACCTCC	AGGGCCCTGG	TCGACCTGCT	GTTTTACGAC	GATACCGTAT
33	2951	CCGGAGCGGC	CGCCGCGTTA	GCCGAGCGCC	CCGCAGAGGA	GTGGCTGGCG
	3001	CGACCCCTGC	CCGAGGGACT	GCAGGCGTTC	GGGGCCGTCC	TCGTAGACGC
60	3051	CCATCGGCGC	ATCACCGACC	: CGGAGAGGGA	CATCCAGGAC	TTTGTCCTCA
	3101	CCGCCGAACT	' GAGCAGACAC	CCGCGCGCGT	ACACCAACAA	GCGCCTGGCC
65	3151	CACCTGACGG	TGTATTACAA	GCTCATGGCC	CGCCGCGCGC	AGGTCCCGTC
65	3201	CATCAAGGAC	CGGATCCCGT	ACGTGATCGT	GGCCCAGACC	CGCGAGGTAG

WO 02/	/06513					PCT/US01/16525
	3251	AGGAGACGGT	CGCGCGGCTG	GCCGCCCTCC	GCGAGCTCGA	CGCCGCCGCC
	3301	CCAGGGGACG	AGCCCGCCCC	CCCCGCGGCC	CTGCCCTCCC	CGGCCAAGCG
5	3351	CCCCCGGGAG	ACGCCGTTGC	ATGCCGACCC	CCCGGGAGGC	GCGTCCAAGC
	3401	CCCGCAAGCT	GCTGGTGTCC	GAGCTGGCCG	AGGATCCCGC	ATACGCCATT
10	3451	GCCCACGGCG	TCGCCCTGAA	CACGGACTAT	TACTTCTCCC	ACCTGTTGGG
10	3501	GGCGGCGTGC	GTGACATTCA	AGGCCCTGTT	TGGGAATAAC	GCCAAGATCA
	3551	CCGAGAGTCT	GTTAAAAAGG	TTTATTCCCG	AAGTGTGGCA	CCCCCGGAC
15	3601	GACGTGGCCG	CGCGGCTCCG	GGCCGCAGGG	TTCGGGGCGG	TGGGTGCCGG
	3651	CGCTACGGCG	GAGGAAACTC	GTCGAATGTT	GCATAGAGCC	TTTGATACTC
	3701	TAGCATGA				

SEO.ID.NO. 8 Amino acid sequence of DNA polymerase for HSV1-F-M1

1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA 5 51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK 101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY 151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG 10 201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA 251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT 301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL 15 351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD 401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF 20 451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR 501 VWDIGOSHFO KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD 551 KKKDLSYRDI PAYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA 25 601 VARLAGINIT RTIYDGOOIR VFTCLLRLAD QKGFILPDTQ GRFRGGGGEA 651 PKRPAAARED EERPEEGED EDEREEGGGE REPEGARETA GRHVGYQGAR 30 701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK 751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA 801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE 35 851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA 901 GLTAVGDKMA SHISRALFLS PIKLECEKTF TKLLLIAKKK YIGVIYGGKM 40 951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA 1001 RPLPEGLOAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA 45 1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA 1101 PGDEPAPPAA LPSPAKRPRE TPLHADPPGG ASKPRKLLVS ELAEDPAYAI 1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD 50 1201 DVAARLRAAG FGAVGAGATA EETRRMLHRA FDTLA\*

SEQ.ID.NO. 9 DNA sequence of HSV polymerase gene for HSV1-DJL-M1

1 ATGTTTCCG GTGGCGGCGG CCCGCTGTCC CCCGGAGGAA AGTCGGCGGC 51 CAGGGCGGCG TCCGGGTTTT TTGCGCCCGC CGGCCCTCGC GGAGCCGGCC 5 101 GGGGACCCCC GCCTTGTTTG AGGCAAAACT TTTACAACCC CTACCTCGCC 151 CCAGTCGGGA CGCAACAGAA GCCGACCGGG CCAACCCAGC GCCATACGTA 10 201 CTATAGCGAA TGCGATGAAT TTCGATTCAT CGCCCCGCGG GTGCTGGACG 251 AGGATGCCCC CCCGGAGAAG CGCGCCGGGG TGCACGACGG TCACCTCAAG 301 CGCGCCCCA AGGTGTACTG CGGGGGGGAC GAGCGCGACG TCCTCCGCGT 15 351 CGGGTCGGGC GGCTTCTGGC CGCGGCGCTC GCGCCTGTGG GGCGGCGTGG 401 ACCACGCCC GGCGGGGTTC AACCCCACG TCACCGTCTT TCACGTGTAT 20 451 GACATCCTGG AGAACGTGGA GCACGCGTAC GGCATGCGCG CGGCCCAGTT 501 CCACGCGCGG TTTATGGACG CCATCACACC GACGGGGACC GTCATCACGC 551 TCCTGGGCCT GACTCCGGAA GGCCACCGGG TGGCCGTTCA CGTTTACGGC 25 601 ACGCGGCAGT ACTTTTACAT GAACAAGGAG GAGGTTGACA GGCACCTACA 651 ATGCCGCGC CCACGAGATC TCTGCGAGCG CATGGCCGCG GCCCTGCGCG 30 701 AGTCCCGGG CGCGTCGTTC CGCGGCATCT CCGCGGACCA CTTCGAGGCG 751 GAGGTGGTGG AGCGCACCGA CGTGTACTAC TACGAGACGC GCCCCGCTCT 801 GTTTTACCGC GTCTACGTCC GAAGCGGGCG CGTGCTGTCG TACCTGTGCG 35 851 ACAACTTCTG CCCGGCCATC AAGAAGTACG AGGGTGGGGT CGACGCCACC 901 ACCCGGTTCA TCCTGGACAA CCCCGGGTTC GTCACCTTCG GCTGGTACCG 40 951 TCTCAAACCG GGCCGGAACA ACACGCTAGC CCAGCCGCGG GCCCCGATGG 1001 CCTTCGGGAC ATCCAGCGAT GTCGAGTTTA ACTGTACGGC GGACAACCTG 1051 GCCATCGAGG GGGGCATGAG CGACCTACCG GCATACAAGC TCATGTGCTT 45 1101 CGATATCGAA TGCAAGGCGG GGGGGGAGGA CGAGCTGGCC TTTCCGGTGG 1151 CCGGGCACCC GGAGGACCTG GTCATCCAGA TATCCTGTCT GCTCTACGAC 50 1201 CTGTCCACCA CCGCCCTGGA GCACGTCCTC CTGTTTTCGC TCGGTTCCTG 1251 CGACCTCCCC GAATCCCACC TGAACGAGCT GGCGGCCAGG GGCCTGCCCA 1301 CGCCCGTGGT TCTGGAATTC GACAGCGAAT TCGAGATGCT GTTGGCCTTC 55 1351 ATGACCCTTG TGAAACAGTA CGGCCCCGAG TTCGTGACCG GGTACAACAT 1401 AATCAACTTC GACTGGCCCT TCTTGCTGGC CAAGCTGACG GACATTTACA

1451 AGGTCCCCT GGACGGGTAC GGCCGCATGA ACGGCCGGGG CGTGTTTCGC 1501 GTGTGGGACA TAGGCCAGAG CCACTTCCAG AAGCGCAGCA AGATAAAGGT 5 1551 GAACGCATG GTGAACATCG ACATGTACGG GATTATAACC GACAAGATCA 1601 AGCTCTCGAG CTACAAGCTC AACGCCGTGG CCGAAGCCGT CCTGAAGGAC 1651 AAGAAGAAGG ACCTGAGCTA TCGCGACATC CCCACCTACT ACGCCGCCGG 10 1701 GCCCGCGCAA CGCGGGGTGA TCGGCGAGTA CTGCATACAG GATTCCCTGC 1751 TGGTGGCCA GCTGTTTTTT AAGTTTTTGC CCCATCTGGA GCTCTCGGCC 15 1801 GTCGCGCGCT TGGCGGGTAT TAACATCACC CGCACCATCT ACGACGGCCA 1851 GCAGATCCGC GTCTTTACGT GCCTGCTGCG CCTGGCCGAC CAGAAGGGCT 20 1901 TTATTCTGCC GGACACCCAG GGGCGATTTA GGGGCGCCGG GGGGGAGGCG 1951 CCCAAGCGTC CGGCCGCAGC CCGGGAGGAC GAGGAGCGGC CAGAGGAGGA 2001 GGGGGAGGAC GAGAACGAAC GCGAGGAGGG CGGGGGCGAG CGGGAGCCGG 25 2051 AGGGCGCGGGGAGACCGCC GGCCGCACG TGGGGTACCA GGGGGCCAGG 2101 GTCCTTGACC CCACTTCCGG GTTTCACGTG AACCCCGTGG TGGTGTTCGA 30 2151 CTTTGCCAGC CTGTACCCCA GCATCATCCA GGCCCACAAC CTGTGCTTCA 2201 GCACGCTCTC CCTGAGGGCC GACGCAGTGG CGCACCTGGA GGCGGGCAAG 2251 GACTACCTGG AGATCGAGGT GGGGGGGGGGA CGGCTGTTCT TCGTCAAGGC 35 2301 TCACGTGCGA GAGAGCCTCC TCAGCATCCT CCTGCGGGAC TGGCTCGCCA 2351 TGCGAAAGCA GATCCGCTCG CGGATTCCCC AGAGCAGCCC CGAGGAGGCC 40 2401 GTGCTCCTGG ACAAGCAGCA GGCCGCCATC AAGGTCGTGT GTAACTCGGT 2451 TTACGGGTTC ACGGGAGCGC AGCACGGACT CCTGCCGTGC CTGCACGTTG 2501 CCGCGACGGT GACGACCATC GGCCGCGAGA TGCTGCTCGC GACCCGCGAG 45 2551 TACGTCCACG CGCGCTGGGC GGCCTTCGAA CAGCTCCTGG CCGATTTCCC 2601 GGAGGCGGCC GACATGCGCG CCCCCGGGCC CTATTCCATG CGCATCATCT 50 2651 ACGGGGACAC GGACTCCATA TTTGTGCTGT GCCGCGGCCT CACGGCCGCC 2701 GGGCTGACGG CCGTGGGCGA CAAGATGGCG AGCCACATCT CGCGCGCGCT 2751 GTTTCTGCCC CCCATCAAAC TCGAGTGCGA AAAGACGTTC ACCAAGCTGC 55 2801 TGCTGATCGC CAAGAAAAG TACATCGGCG TCATCTACGG GGGTAAGATG 2851 CTCATCAAGG GCGTGGATCT GGTGCGCAAA AACAACTGCG CGTTTATCAA 2901 CCGCACCTCC AGGGCCCTGG TCGACCTGCT GTTTTACGAC GATACCGTAT 60

	2951 CCGGAGCGGC CGCCGCGTTA GCCGAGCGCC CCGCAGAGGA GTGGCTGGCG
5	3001 CGACCCCTGC CCGAGGGACT GCAGGCGTTC GGGGCCGTCC TCGTAGACGC
3	3051 CCATCGGCGC ATCACCGACC CGGAGAGGGA CATCCAGGAC TTTGTTCTCA
	3101 CCGCCGAACT GAGCAGACAC CCGCGCGCGT ACACCAACAA GCGCCTGGCC
10	3151 CACCTGACGG TGTATTACAA GCTCATGGCC CGCCGCGCGC AGGTCCCGTC
	3201 CATCAAGGAC CGGATCCCGT ACGTGATCGT GGCCCAGACC CGCGAGGTAG
15	3251 AGGAGACGGT CGCGCGGCTG GCCGCCCTCC GCGAGCTAGA CGCCGCCGCC
13	3301 CCAGGGGACG AGCCCGCCCC CCCCGCGGCC CTGCCCTCCC CGGCCAAGCG
	3351 CCCCCGGGAG ACGCCGTCGC CTGCCGACCC CCCGGGAGGC GCGTCCAAGC
20	3401 CCCGCAAGCT GCTGGTGTCC GAGCTGGCCG AGGATCCCGC ATACGCCATT
	3451 GCCCACGGCG TCGCCCTGAA CACGGACTAT TACTTCTCCC ACCTGTTGGG
25	3501 GGCGGCGTGC GTGACATTCA AGGCCCTGTT TGGGAATAAC GCCAAGATCA
23	3551 CCGAGAGTCT GTTAAAAAGG TTTATTCCCG AAGTGTGGCA CCCCCCGGAC
	3601 GACGTGGCCG CGCGGCTCCG GACCGCAGGG TTCGGGGCGG TGGGTGCCGG
30	3651 CGCTACGGCG GAGGAAACTC GTCGAATGTT GCATAGAGCC TTTGATACTC
	3701 TAGCATGA

**SEQ.ID.NO. 10** Amino acid sequence of DNA polymerase for HSV1-DJL-M1

	1 MFSGGGGPLS PGGKSAARAA SGFFAPAGPR GAGRGPPPCL RQNFYNPYLA
5	51 PVGTQQKPTG PTQRHTYYSE CDEFRFIAPR VLDEDAPPEK RAGVHDGHLK
	101 RAPKVYCGGD ERDVLRVGSG GFWPRRSRLW GGVDHAPAGF NPTVTVFHVY
10	151 DILENVEHAY GMRAAQFHAR FMDAITPTGT VITLLGLTPE GHRVAVHVYG
10	201 TRQYFYMNKE EVDRHLQCRA PRDLCERMAA ALRESPGASF RGISADHFEA
	251 EVVERTDVYY YETRPALFYR VYVRSGRVLS YLCDNFCPAI KKYEGGVDAT
15	301 TRFILDNPGF VTFGWYRLKP GRNNTLAQPR APMAFGTSSD VEFNCTADNL
	351 AIEGGMSDLP AYKLMCFDIE CKAGGEDELA FPVAGHPEDL VIQISCLLYD
20	401 LSTTALEHVL LFSLGSCDLP ESHLNELAAR GLPTPVVLEF DSEFEMLLAF
20	451 MTLVKQYGPE FVTGYNIINF DWPFLLAKLT DIYKVPLDGY GRMNGRGVFR
	501 VWDIGQSHFQ KRSKIKVNGM VNIDMYGIIT DKIKLSSYKL NAVAEAVLKD
25	551 KKKDLSYRDI PTYYAAGPAQ RGVIGEYCIQ DSLLVGQLFF KFLPHLELSA
	601 VARLAGINIT RTIYDGQQIR VFTCLLRLAD QKGFILPDTQ GRFRGAGGEA
30	651 PKRPAAARED EERPEEEGED ENEREEGGGE REPEGARETA GRHVGYQGAR
50	701 VLDPTSGFHV NPVVVFDFAS LYPSIIQAHN LCFSTLSLRA DAVAHLEAGK
	751 DYLEIEVGGR RLFFVKAHVR ESLLSILLRD WLAMRKQIRS RIPQSSPEEA
35	801 VLLDKQQAAI KVVCNSVYGF TGAQHGLLPC LHVAATVTTI GREMLLATRE
	851 YVHARWAAFE QLLADFPEAA DMRAPGPYSM RIIYGDTDSI FVLCRGLTAA
40	901 GLTAVGDKMA SHISRALFLP PIKLECEKTF TKLLLIAKKK YIGVIYGGKM
10	951 LIKGVDLVRK NNCAFINRTS RALVDLLFYD DTVSGAAAAL AERPAEEWLA
	1001 RPLPEGLQAF GAVLVDAHRR ITDPERDIQD FVLTAELSRH PRAYTNKRLA
45	1051 HLTVYYKLMA RRAQVPSIKD RIPYVIVAQT REVEETVARL AALRELDAAA
	1101 PGDEPAPPAA LPSPAKRPRE TPSPADPPGG ASKPRKLLVS ELAEDPAYAI
50	1151 AHGVALNTDY YFSHLLGAAC VTFKALFGNN AKITESLLKR FIPEVWHPPD
	1201 DVAARLRTAG FGAVGAGATA EETRRMLHRA FDTLA*

SEQ.ID.NO. 11 DNA sequence of DNA polymerase gene for HMCV-AD169-M1

1 ATGTTTTCA ACCCGTATCT GAGCGGCGC GTGACCGGCG GTGCGGTCGC 51 GGGTGGCCGG CGTCAGCGTT CGCAGCCCGG CTCCGCGCAG GGCTCGGGCA 5 101 AGCGGCCGCC ACAGAAACAG TTTTTGCAGA TCGTGCCGCG AGGTGTCATG 151 TTCGACGGTC AGACGGGGTT GATCAAGCAT AAGACGGGAC GGCTGCCTCT 10 201 CATGTTCTAT CGAGAGATTA AACATTTGTT GAGTCATGAC ATGGTTTGGC 251 CGTGTCCTTG GCGCGAGACC CTGGTGGGTC GCGTGGTGGG ACCTATTCGT 301 TTTCACACCT ACGATCAGAC GGACGCCGTG CTCTTCTTCG ACTCGCCCGA 15 351 AAACGTGTCG CCGCGCTATC GTCAGCATCT GGTGCCTTCG GGGAACGTGT 401 TGCGTTTCTT CGGGGCCACA GAACACGGCT ACAGTATCTG CGTCAACGTT 20 451 TTCGGGCAGC GCAGCTACTT TTACTGTGAG TACAGCGACA CCGATAGGCT 501 GCGTGAGGTC ATTGCCAGCG TGGGCGAACT AGTGCCCGAA CCGCGGACGC 551 CATACGCCGT GTCTGTCACG CCGGCCACCA AGACCTCCAT CTATGGGTAC 25 601 GGGACGCGAC CCGTGCCCGA TTTGCAGTGT GTGTCTATCA GCAACTGGAC 651 CATGGCCAGA AAAATCGGCG AGTATCTGCT GGAGCAGGGT TTTCCCGTGT 30 701 ACGAGGTCCG TGTGGATCCG CTGACGCGTT TGGTCATCGA TCGGCGGATC 751 ACCACGTTCG GCTGGTGCTC CGTGAATCGT TACGACTGGC GGCAGCAGGG 801 TCGCGCGTCG ACTTGTGATA TCGAGGTAGA CTGCGATGTC TCTGACCTGG 35 851 TGGCTGTGCC CGACGACAGC TCGTGGCCGC GCTATCGATG CCTGTCCTTC 901 GATATCGAGT GCATGAGCGG CGAGGGTGGT TTTCCCTGCG CCGAGAAGTC 40 951 CGATGACATT GTCATTCAGA TCTCGTGCGT GTGCTACGAG ACGGGGGGAA 1001 ACACCGCCGT GGATCAGGGG ATCCCAAACG GGAACGATGG TCGGGGCTGC 1051 ACTTCGGAGG GTGTGATCTT TGGGCACTCG GGTCTTCATC TCTTTACGAT 45 1101 CGGCACCTGC GGGCAGGTGG GCCCAGACGT GGACGTCTAC GAGTTCCCTT 1151 CCGAATACGA GCTGCTGCTG GGCTTTATGC TTTTCTTTCA ACGGTACGCG 50 1201 CCGGCCTTTG TGACCGGTTA CAACATCAAC TCTTTTGACT TGAAGTACAT 1251 CCTCACGCGT CTCGAGTACC TGTATAAGGT GGACTCGCAG CGCTTCTGCA 1301 AGTTGCCTAC GGCGCAGGGC GGCCGTTTCT TTTTACACAG CCCCGCCGTG 55 1351 GGTTTTAAGC GGCAGTACGC CGCCGCTTTT CCCTCGGCTT CTCACAACAA 1401 TCCGGCCAGC ACGGCCGCCA CCAAGGTGTA TATTGCGGGT TCGGTGGTTA

	1451 TCGACATGTA CCCTGTATGC ATGGCCAAGA CTAACTCGCC CAACTATAAG
. 5	1501 CTCAACACTA TGGCCGAGCT TTACCTGCGG CAACGCAAGG ATGACCTGTC
	1551 TTACAAGGAC ATCCCGCGTT GTTTCGTGGC TAATGCCGAG GGCCGCCCC
	1601 AGGTAGGCCG TTACTGTCTG CAGGACGCCG TATTGGTGCG CGATCTGTTC
10	1651 AACACCATTA ATTTTCACTA CGAGGCCGGG GCCATCGCGC GGCTGGCTAA
	1701 AATTCCGTTG CGGCGTGTCA TCTTTGACGG ACAGCAGATC CGTATCTACA
15	1751 CCTCGCTGCT GGACGAGTGC GCCTGCCGCG ATTTTATCCT GCCCAACCAC
13	1801 TACAGCAAAG GTACGACGGT GCCCGAAACG AATAGCGTTG CTGTGTCACC
	1851 TAACGCTGCT ATCATCTCTA CCGCCGCTGT GCCCGGCGAC GCGGGTTCTG
20	1901 TGGCGGCTAT GTTTCAGATG TCGCCGCCCT TGCAATCTGC GCCGTCCAGT
-	1951 CAGGACGGCG TTTCACCCGG CTCCGGCAGT AACAGTAGTA GCAGCGTCGG
25	2001 CGTTTTCAGC GTCGGCTCCG GCAGTAGTGG CGGCGTCGGC GTTTCCAACG
23.	2051 ACAATCACGG CGCCGGCGGT ACTGCGGCGG TTTCGTACCA GGGCGCCACG
	2101 GTGTTTGAGC CCGAGGTGGG TTACTACAAC GACCCCGTGG CCGTGTTCGA
30	2151 CTTTGCCAGC CTCTACCCTT CCATCATCAT GGCCCACAAC CTCTGCTACT
	2201 CCACCCTGCT GGTGCCGGGT GGCGAGTACC CTGTGGACCC CGCCGACGTA
35	2251 TACAGCGTCA CGCTAGAGAA CGGCGTGACC CACCGCTTTG TGCGTGCTTC
33	2301 GGTGCGCGTC TCGGTGCTCT CGGAACTGCT CAACAAGTGG GTTTCGCAGC
	2351 GGCGTGCCGT GCGCGAATGC ATGCGCGAGT GTCAAGACCC TGTGCGCCGT
40	2401 ATGCTGCTCG ACAAGGAACA GATGGCGCTC AAAGTAACGT GCAACGCTTT
	2451 CTACGGTTTT ACCGGCGCGC TGAACGGTAT GATGCCGTGT CTGCCCATCG
45	2501 CCGCCAGCAT CACGCGCATC GGTCGCGACA TGCTAGAGCG CACGGCGCGG
43	2551 TTCATCAAAG ACAACTTTTC AGAGCCGTGT TTTTTGCACA ATTTTTTAA
	2601 TCAGGAAGAC TATGTAGTGG GAACGCGGGA GGGGGATTCG GAGGAGAGCA
50	2651 GCGCGTTACC GGAGGGGCTC GAAACATCGT CAGGGGGCTC GAACGAACGG
	2701 CGGGTGGAGG CGCGGGTCAT CTACGGGGAC ACGGACAGCG TGTTTGTCCG
<i>55</i>	2751 CTTTCGTGGC CTGACGCCGC AGGCTCTGGT GGCGCGTGGG CCCAGCCTGG
55	2801 CGCACTACGT GACGGCCTGT CTTTTTGTGG AGCCCGTCAA GCTGGAGTTT
,	2851 GAAAAGGTCT TCGTCTCTCT TATGATGATC TGCAAGAAAC GTTACATCGG
60	2901 CAAAGTGGAG GGCGCCTCGG GTCTGAGCAT GAAGGGCGTG GATCTGGTGC

	2951	GCAAGACGGC CTGCGAGTTC GTCAAGGGCG TCACGCGTGA CGTCCTCTCG
5	3001	CTGCTCTTTG AGGATCGCGA GGTCTCGGAA GCAGCCGTGC GCCTGTCGCG
3	3051	CCTCTCACTC GATGAAGTCA AGAAGTACGG CGTGCCACGC GGTTTCTGGC
	3101	GTATCTTACG CCGCTTGGTG CAGGCCCGCG ACGATCTGTA CCTGCACCGT
0	3151	GTGCGTGTCG AGGACCTGGT GCTTTCGTCG GTGCTCTCTA AGGACATCTC
	3201	GCTGTACCGT CAATCTAACC TGCCGCACAT TGCCGTCATT AAGCGATTGG
15	3251	CGGCCCGTTC TGAGGAGCTA CCCTCGGTCG GGGATCGGGT CTTTTACGTT
13	3301	CTGACGGCGC CCGGTGTCCG GACGGCGCCG CAGGGTTCCT CCGACAACGG
	3351	TGATTCTGTA ACCGCCGGCG TGGTTTCCCG GTCGGACGCG ATTGATGGCA
20	3401	CGGACGACGA CGCTGACGGC GGCGGGGTAG AGGAGAGCAA CAGGAGAGGA
	3451	GGAGAGCCGG CAAAGAAGAG GGCGCGGAAA CCACCGTCGG CCGTGTGCAA
25	3501	CTACGAGGTA GCCGAAGATC.CGAGCTACGT GCGCGAGCAC GGCGTGCCCA
2.5	3551	TTCACGCCGA CAAGTACTTT GAGCAGGTTC TCAAGGCTGT AACTAACGTG
	3601	CTGTCGCCCG TCTTTCCCGG CGGCGAAACC GCGCGCAAGG ACAAGTTTTT
30	3651	GCACATGGTG CTGCCGCGGC GCTTGCACTT GGAGCCGGCT TTTCTGCCGT
	3701	ACAGTGTCAA GGCGCACGAA TGCTGTTGA

### SEQ.ID.NO.12 Amino acid sequence of DNA polymerase for HCMV-AD169-M1

_	1 MFFNPYLSGG VTGGAVAGGR RQRSQPGSAQ GSGKRPPQKQ FLQIVPRGVM
5	51 FDGQTGLIKH KTGRLPLMFY REIKHLLSHD MVWPCPWRET LVGRVVGPIR
	101 FHTYDQTDAV LFFDSPENVS PRYRQHLVPS GNVLRFFGAT EHGYSICVNV
10	151 FGQRSYFYCE YSDTDRLREV IASVGELVPE PRTPYAVSVT PATKTSIYGY
	201 GTRPVPDLQC VSISNWTMAR KIGEYLLEQG FPVYEVRVDP LTRLVIDRRI
15	251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF
15	301 DIECMSGEGG FPCAEKSDDI VIQISCVCYE TGGNTAVDQG IPNGNDGRGC
	351 TSEGVIFGHS GLHLFTIGTC GQVGPDVDVY EFPSEYELLL GFMLFFQRYA
20	401 PAFVTGYNIN SFDLKYILTR LEYLYKVDSQ RFCKLPTAQG GRFFLHSPAV
	451 GFKRQYAAAF PSASHNNPAS TAATKVYIAG SVVIDMYPVC MAKTNSPNYK
25	501 LNTMAELYLR QRKDDLSYKD IPRCFVANAE GRAQVGRYCL QDAVLVRDLF
23	551 NTINFHYEAG AIARLAKIPL RRVIFDGQQI RIYTSLLDEC ACRDFILPNH
	601 YSKGTTVPET NSVAVSPNAA IISTAAVPGD AGSVAAMFQM SPPLQSAPSS
30	651 QDGVSPGSGS NSSSSVGVFS VGSGSSGGVG VSNDNHGAGG TAAVSYQGAT
	701 VFEPEVGYYN DPVAVFDFAS LYPSIIMAHN LCYSTLLVPG GEYPVDPADV
35	751 YSVTLENGVT HRFVRASVRV SVLSELLNKW VSQRRAVREC MRECQDPVRR
55	801 MLLDKEQMAL KVTCNAFYGF TGALNGMMPC LPIAASITRI GRDMLERTAR
	851 FIKDNFSEPC FLHNFFNQED YVVGTREGDS EESSALPEGL ETSSGGSNER
40	901 RVEARVIYGD TDSVFVRFRG LTPQALVARG PSLAHYVTAC LFVEPVKLEF
	951 EKVFVSLMMI CKKRYIGKVE GASGLSMKGV DLVRKTACEF VKGVTRDVLS
45	1001 LLFEDREVSE AAVRLSRLSL DEVKKYGVPR GFWRILRRLV QARDDLYLHR
-15	1051 VRVEDLVLSS VLSKDISLYR QSNLPHIAVI KRLAARSEEL PSVGDRVFYV
	1101 LTAPGVRTAP QGSSDNGDSV TAGVVSRSDA IDGTDDDADG GGVEESNRRO
50	1151 GEPAKKRARK PPSAVCNYEV AEDPSYVREH GVPIHADKYF EQVLKAVTNV
	1201 LSPVFPGGET ARKDKFLHMV LPRRLHLEPA FLPYSVKAHE CC*

# Figure 6 SEQ.ID.NO.13 Amino acid sequence of DNA polymerase for HCMV-AD169

1 MFFNPYLSGG VTGGAVAGGR RQRSQPGSAQ GSGKRPPQKQ FLQIVPRGVM 5 51 FDGQTGLIKH KTGRLPLMFY REIKHLLSHD MVWPCPWRET LVGRVVGPIR 101 FHTYDQTDAV LFFDSPENVS PRYRQHLVPS GNVLRFFGAT EHGYSICVNV 10 151 FGORSYFYCE YSDTDRLREV IASVGELVPE PRTPYAVSVT PATKTSIYGY 201 GTRPVPDLQC VSISNWTMAR KIGEYLLEQG FPVYEVRVDP LTRLVIDRRI 251 TTFGWCSVNR YDWRQQGRAS TCDIEVDCDV SDLVAVPDDS SWPRYRCLSF 15 301 DIECMSGEGG FPCAEKSDDI VIQISCVCYE TGGNTAVDQG IPNGNDGRGC 351 TSEGVIFGHS GLHLFTIGTC GOVGPDVDVY EFPSEYELLL GFMLFFQRYA 20 401 PAFVTGYNIN SFDLKYILTR LEYLYKVDSQ RFCKLPTAQG GRFFLHSPAV 451 GFKROYAAAF PSASHNNPAS TAATKVYIAG SVVIDMYPVC MAKTNSPNYK 501 LNTMAELYLR QRKDDLSYKD IPRCFVANAE GRAQVGRYCL QDAVLVRDLF 25 551 NTINFHYEAG AIARLAKIPL RRVIFDGQQI RIYTSLLDEC ACRDFILPNH 601 YSKGTTVPET NSVAVSPNAA IISTAAVPGD AGSVAAMFQM SPPLQSAPSS 30 651 QDGVSPGSGS NSSSSVGVFS VGSGSSGGVG VSNDNHGAGG TAAVSYQGAT 701 VFEPEVGYYN DPVAVFDFAS LYPSIIMAHN LCYSTLLVPG GEYPVDPADV 751 YSVTLENGVT HRFVRASVRV SVLSELLNKW VSQRRAVREC MRECQDPVRR 35 801 MLLDKEQMAL KVTCNAFYGF TGVVNGMMPC LPIAASITRI GRDMLERTAR 851 FIKDNFSEPC FLHNFFNQED YVVGTREGDS EESSALPEGL ETSSGGSNER 40 901 RVEARVIYGD TDSVFVRFRG LTPQALVARG PSLAHYVTAC LFVEPVKLEF 951 EKVFVSLMMI CKKRYIGKVE GASGLSMKGV DLVRKTACEF VKGVTRDVLS 1001 LLFEDREVSE AAVRLSRLSL DEVKKYGVPR GFWRILRRLV QARDDLYLHR 45 1051 VRVEDLVLSS VLSKDISLYR QSNLPHIAVI KRLAARSEEL PSVGDRVFYV 1101 LTAPGVRTAP QGSSDNGDSV TAGVVSRSDA IDGTDDDADG GGVEESNRRG 50 1151 GEPAKKRARK PPSAVCNYEV AEDPSYVREH GVPIHADKYF EQVLKAVTNV 1201 LSPVFPGGET ARKDKFLHMV LPRRLHLEPA FLPYSVKAHE CC\*

#### SEQUENCE LISTING

Wather Hopkir	<pre>110&gt; Homa, Fred Wathen, Michael Hopkins, Todd Thomsen, Darrell</pre>												
<120> A Me	thod for Tr	reating Herp	oes Virus										
<130> 0022	1												
<160> 19	160> 19												
<170> PatentIn version 3.0													
<210> 1 <211> 3717 <212> DNA <213> herpes simplex													
<400> 1 atgttttgtg (	ccacaaacaa	cccgacttcc	cccaaaaaaa	agtcggcggc	tcaaacaaca	60							
tctgggtttt						120							
cgccggcaga a						180							
gggccggctc a						240							
cgttcgctgg a	acgaggacgc	ccccgcggag	cagcgcaccg	gggtccacga	cggccgcctc	300							
cggcgcgccc (	ctaaggtgta	ctgcgggggg	gacgagcgcg	acgtcctccg	cgtgggcccg	360							
gagggcttct g	ggccgcgtcg	cttgcgcctg	tggggcggtg	cggaccatgc	ccccaagggg	420							
ttcgacccca (	ccgtcaccgt	cttccacgtg	tacgacatcc	tggagcacgt	ggaacacgcg	480							
tacagcatgc g	gcgccgccca	gctccacgag	cgatttatgg	acgccatcac	gcccgccggg	540							
accgtcatca c	cgcttctggg	tctgaccccc	gaaggccatc	gcgtcgccgt	tcacgtctac	600							
ggcacgcggc a	agtactttta	catgaacaag	gcggaggtgg	atcggcacct	gcagtgccgt	660							
gccccgcgcg a	atctctgcga	gcgcctggcg	gcggccctgc	gcgagtcgcc	gggggcgtcg	720							
ttccgcggca	tctccgcgga	ccacttcgag	gcggaggtgg	tggagcgcgc	cgacgtgtac	780							
tattacgaaa o	cgcgcccgac	cctgtactac	cgcgtcttcg	tgcgaagcgg	gcgcgcgctg	840							
gcctacctgt q	gcgacaactt	ttgccccgcg	atcaggaagt	acgagggggg	cgtcgacgcc	900							
accacccggt	ttatcctgga	caacccgggg	tttgtcacct	tcggctggta	ccgcctcaag	960							
cccggccgcg (	ggaacgcgcc	ggcccaaccg	cgccccccga	cggcgttcgg	aacctcgagc	1020							
gacgtcgagt	ttaactgcac	ggcggacaac	ctggccgtcg,	agggggccat	gtgtgacctg	1080							
ccggcctaca a	agctcatgtg	cttcgatatc	gaatgcaagg	.ccggggggga	ggacgagctg	1140							
gcctttccgg (	tegeggaaeg	cccggaagac	ctcgtcatcc"	agateteetg	tctgctctac	1200							
gacctgtcca d	ccaccaccct	cgaggagate	ctcctatttt	cactcagate	ctgcgacctc	1260							

cccgagtccc	acctcagcga	tetegeetee	aggggcctgc	cggcccccgt	cgtcctggag	1320
tttgacagcg	aattcgagat	gctgctggcc	ttcatgacct	tcgtcaagca	gtacggcccc	1380
gagttcgtga	ccgggtacaa	catcatcaac	ttcgactggc	ccttcgtcct	gaccaagctg	1440
acggagatct	acaaggteee	gctcgacggg	tacgggcgca	tgaacggccg	gggtgtgttc	1500
cgcgtgtggg	acatcggcca	gagccacttt	cagaagcgca	gcaagatcaa	ggtgaacggg	1560
atggtgaaca	tcgacatgta	cggcatcatc	accgacaagg	tcaaactctc	cagctacaag	1620
ctgaacgccg	tegeegagge	cgtcttgaag	gacaagaaga	aggatctgag	ctaccgcgac	1680
atccccgcct	actacgcctc	cgggcccgcg	cagcgcgggg	tgatcggcga	gtattgtgtg	1740
caggactcgc	tgctggtcgg	gcagctgttc	ttcaagtttc	tgccgcacct	ggagctttcc	1800
gccgtcgcgc	gcctggcggg	catcaacatc	acccgcacca	tctacgacgg	ccagcagatc	1860
cgcgtcttca	cgtgcctcct	gcgccttgcg	ggccagaagg	gcttcatcct	gccggacacc	1920
caggggcggt	ttcggggcct	cgacaaggag	gcgcccaagc	gcccggccgt	gcctcggggg .	1980
gaaggggagc	ggccggggga	cgggaacggg	gacgaggata	aggacgacga	cgaggacgag	2040
gacggggacg	agcgcgagga	ggtcgcgcgc	gagaccgggg	gccggcacgt	tgggtaccag	2100
ggggcccggg	tectegacee	cacctccggg	tttcacgtcg	accccgtggt	ggtgtttgac	2160
tttgccagcc	tgtaccccag	catcatccag	gcccacaacc	tgtgcttcag	tacgctctcc	2220
ctgcggcccg	aggccgtcgc	gcacctggag	gcggaccggg	actacctgga	gatcgaggtg	2280
gggggccgac	ggctgttctt	cgtgaaggcc	cacgtacgcg	agagcctgct	gagcatcctg	2340
ctgcgcgact	ggctggccat	gcgaaagcag	atccgctcgc	ggatccccca	gagcaccccc	2400
gaggaggccg	teeteetega	caagcaacag	gccgccatca	aggtggtgtg	caactcggtg	2460
tacgggttca	ccggggcgca	gcacggtctt	ctgccctgcc	tgcacgtggc	cgccaccgtg	2520
acgaccatcg	gccgcgagat	getectegeg	acgcgcgcgt	acgtgcacgc	gegetgggeg	2580
gagttcgatc	agctgctggc	cgactttccg	gaggcggccg	gcatgcgcgc	ccccggtccg	2640
tactccatgc	gcatcatcta	cggggacacg	gactccattt	tcgttttgtg	ccgcggcctc	2700
acggccgcgg	gcctggtggc	catgggcgac	aagatggcga	gccacatctc	gcgcgcgctg	2760
ttectecccc	cgatcaagct	cgagtgcgaa	aaaacgttca	ccaagctgct	gctcatcgcc	2820
aagaaaaagt	acatcggcgt	catctgcggg	ggcaagatgc	tcatcaaggg	cgtggatctg	2880
gtgcgcaaaa	acaactgcgc	gtttatcaac	cgcacctcca	gggccctggt	cgacctgctg	2940
ttttacgacg	ataccgtatc	cggagcggcc	gccgcgttag	ccgagcgccc	cgcagaggag	3000
tggctggcgc	gacccctgcc	cgagggactg	caggcgttcg	gggccgtcct	cgtagacgcc	3060
catcggcgca	tcaccgaccc	ggagagggac	atccaggact	ttgtcctcac	cgccgaactg	3120

agcagacacc	cgcgcgcgta	caccaacaag	cgcctggccc	acctgacggt	gtattacaag	3180
ctcatggccc	gccgcgcgca	ggtcccgtcc	atcaaggacc	ggatcccgta	cgtgatcgtg	3240
gcccagaccc	gcgaggtaga	ggagacggtc	gcgcggctgg	ccgccctccg	cgagctagac	3300
gccgccgccc	caggggacga	gcccgccccc	ccagcggccc	tgccctcccc	ggccaagcgc	3360
ccccgggaga	cgccgtcgca	tgccgacccc	ccgggaggcg	cgtccaagcc	ccgcaagctg	3420
ctggtgtccg	agctggcgga	ggatcccggg	tacgccatcg	cccggggcgt	tccgctcaac	3480
acggactatt	acttctcgca	cctgctgggg	gcggcctgcg	tgacgttcaa	ggccctgttt	3540
ggaaataacg	ccaagatcac	cgagagtctg	ttaaagaggt	ttattcccga	gacgtggcac	3600
ccccggacg	acgtggccgc	gcggctcagg	gccgcggggt	tegggeegge	gggggccggc	3660
gctacggcgg	aggaaactcg	tcgaatgttg	catagagcct	ttgatactct	agcatga	3717

<sup>&</sup>lt;210> 2

<400> 2

Met Phe Cys Ala Ala Gly Gly Pro Thr Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala 20 25 30

Thr Gln Thr Ala Pro Pro Pro Cys Arg Gln Asn Phe Tyr Asn Pro 35 40 45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln 50 55 60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro 65 70 75 80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
85 90 95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu 100 105 110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu 115 120 125

Arg Leu Trp Gly Gly Ala Asp His Ala Pro Lys Gly Phe Asp Pro Thr 130 135 140

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala 145 150 155 160

Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile 165 170 175

<sup>&</sup>lt;211> 1238

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

Thr Pro Al	a Gly Thr 180	· Val Ile	e Thr	Leu 185	Leu	Gly	Leu	Thr	Pro 190	Glu	Gly
His Arg Va 19		His Va	Tyr 200	Gly	Thr	Arg	Gln	Tyr 205	Phe	Tyr	Met
Asn Lys Al 210	a Glu Val	Asp Arg		Leu	Gln	Cys	Arg 220	Ala	Pro	Arg	Asp
Leu Cys Gl 225	ı Arg Lev	Ala Ala 230	a Ala	Leu	Arg	Glu 235	Ser	Pro	Gly	Ala	Ser 240
Phe Arg Gl	y Ile Ser 245		His	Phe	Glu 250	Ala	Glu	Val	Val	Glu 255	Arg
Ala Asp Va	l Tyr Tyr 260	Tyr Gli	1 Thr	Arg 265	Pro	Thr	Leu	Tyr	Tyr 270	Arg	Val
Phe Val Ar 27		r Arg Ala	Leu 280	Ala	Tyr	Leu	Cys	Asp 285	Asn	Phe	Cys
Pro Ala Il 290	e Arg Lys	Tyr Glu 29!		Gly	Val	Asp	Ala 300	Thr	Thr	Arg	Phe
Ile Leu As 305	p Asn Pro	Gly Pho	e Val	Thr	Phe	Gly 315	Trp	Tyr	Arg	Leu	Lys 320
Pro Gly Ar	g Gly Asr 325		Ala	Gln	Pro 330	Arg	Pro	Pro	Thr	Ala 335	Phe
Gly Thr Se	r Ser Asp 340	Val Glı	ı Phe	Asn 345	Cys	Thr	Ala	Asp	Asn 350	Leu	Ala
Val Glu Gl 35		: Cys Ası	) Leu 360	Pro	Ala	Tyr	Lys	Leu 365	Met	Cys	Phe
Asp Ile Gl 370	u Cys Lys	Ala Gly		Glu	Asp	Glu	Leu 380	Ala	Phe	Pro	Val
Ala Glu Ar 385	g Pro Glu	a Asp Lei 390	ı Val	Ile	Gln	Ile 395	Ser	Cys	Leu	Leu	Туr 400
Asp Leu Se	r Thr Thr 405		ı Glu	His	Ile 410	Leu	Leu	Phe	Ser	Leu 415	Gly
Ser Cys As	p Leu Pro 420	o Glu Se:	: His	Leu 425	Ser	Asp	Leu	Ala	Ser 430	Arg	Gly
Leu Pro Al 43		. Val Le	1 Glu 440	Phe	Asp	Ser	Glu	Phe 445	Glu	Met	Leu
Leu Ala Ph 450	e Met Thi	Phe Val		Gln	Tyr	Gly	Pro 460	Glu	Phe	Val	Thr
Gly Tyr As 465	n Ile Ile	Asn Pho	e Asp	Trp	Pro	Phe 475	Val	Leu	Thr	Lys	Leu 480
Thr Glu Il	e Tyr Lys 485		) Leu	Asp	Gly 490	Tyr	Gly	Arg	Met	Asn 495	Gly
Arg Gly Va	l Phe Arg 500	y Val Tr	Asp	Ile 505	Gly	Gln	Ser	His	Phe 510	Gln	Lys

Arg	Ser	Lys 515	Ile	Lys	Val	Asn	Gly 520	Met	Val	Asn	Ile	Asp 525	Met	Tyr	Gly
Ile	Ile 530	Thr	Asp	Lys	Val	Lys 535	Leu	Ser	Ser	Tyr	Lys 540	Leu	Asn	Ala	Val
Ala 545	Glu	Ala	Val	Leu	Lys 550	Asp	Lys	Lys	Lys	Asp 555	Leu	Ser	Tyr	Arg	Asp 560
Ile	Pro	Ala	Tyr	Туr 565	Ala	Ser	Gly	Pro	Ala 570	Gln	Arg	Gly	Val	Ile 575	Gly
Glu	Tyr	Cys	Val 580	Gĺn	Asp	Ser	Leu	Leu 585	Val	Gly	Gln	Leu	Phe 590	Phe	Lys
Phe	Leu	Pro 595	His	Leu	Glu	Leu	Ser 600	Ala	Val	Ala	Arg	Leu 605	Ala	Gly	Ile
Asn	Ile 610	Thr	Arg	Thr	Ile	Tyr 615	Asp	Gly	Gln	Gln	Ile 620	Arg	Val	Phe	Thr
Cys 625	Leu	Leu	Arg	Leu	Ala 630	Gly	Gln	Lys	Gly	Phe 635	Ile	Leu	Pro	Asp	Thr 640
Gln	Gly	Arg	Phe	Arg 645	Gly	Leu	Asp	Lys	Glu 650	Ala	Pro	Lys	Arg	Pro 655	Ala
Val	Pro	Arg	Gly 660	Glu	Gly	Glu	Arg	Pro 665	Gly	Asp	Gly	Asn	Gly 670	Asp	Glu
Asp	Lys	Asp 675	Asp	Asp	Glu	Asp	Glu 680	Asp	Gly	Asp	Glu	Arg 685	Glu	Glu	Val
Ala	Arg 690	Glu	Thr	Gly	Gly	Arg 695	His	Val	Gly	Tyr	Gln 700	Gly	Ala	Arg	Val
Leu 705	Asp	Pro	Thr	Ser	Gly 710	Phe	His	Val	Asp	Pro 715	Val	Val	Val	Phe	Asp 720
Phe	Ala	Ser	Leu	Tyr 725	Pro	Ser	Ile	Ile	Gln 730	Ala	His	Asn	Leu	Суs 735	Phe
Ser	Thr	Leu	Ser 740	Leu	Arg	Pro	Glu	Ala 745	Val	Ala	His	Leu	Glu 750	Ala	Asp
Arg	Asp	Tyr 755	Leu	Glu	Ile	Glu	Val 760	Gly	Gly	Arg	Arg	Leu 765	Phe	Phe	Val
Lys	Ala 770	His	Val	Arg	Glu	Ser 775	Leu	Leu	Ser	Ile	Leu 780	Leu	Arg	Asp	Trp
785					Gln 790					795				•	800
Glu	Glu	Ala	Val	Leu 805	Leu	Asp	Lys	Gln	Gln 810		Ala	Ile	Lys	Val 815	Val
			820		Gly			825					830		
Cys	Leu	His	Val	Ala	Ala	Thr	Val	Thr	Thr	Ile	${\tt Gly}$	Arg	Glu	Met	Leu

835 840 845

- Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe Asp Gln 850 855
- Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro Gly Pro 865 870 875 880
- Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu 885 890 895
- Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met 900 905 910
- Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu 915 920 925
- Cys Glu Lys Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Tyr 930 940
- Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu 945 950 955 960
- Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu 965 970 975
- Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala 980 985 990
- Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu 995 1000 1005
- Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg 1010 1015 1020
- Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala 1025 1030 1035
- Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala 1040 1045 1050
- His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val 1055 1060 1065
- Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr 1070 1075 1080
- Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu 1085 1090 1095
- Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala 1100 1105 1110
- Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala 1115 1120 1125
- Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser 1130 1135 1140
- Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly Val Pro 1145 1150 1155

Leu Asn Thr Asp Tyr Ty 1160	r Phe Ser His 1165	Leu Leu Gly Ala 1170	Ala Cys
Val Thr Phe Lys Ala Le	u Phe Gly Asr 1180	Asn Ala Lys Ile 1185	Thr Glu
Ser Leu Leu Lys Arg Ph 1190	e Ile Pro Glu 1195	Thr Trp His Pro	Pro Asp
Asp Val Ala Ala Arg Le 1205	u Arg Ala Ala 1210	Gly Phe Gly Pro 1215	Ala Gly
Ala Gly Ala Thr Ala Gl 1220	u Glu Thr Arg 1225	Arg Met Leu His 1230	Arg Ala
Phe Asp Thr Leu Ala 1235			
<210> 3 <211> 3723 <212> DNA <213> herpes simplex			
<400> 3 atgttttgtg ccgcgggcgg c	ccggcttcc cccg	ggggga agteggegge	tegggeggeg 60
tctgggtttt ttgccccca c	aacccccgg ggag	ccaccc agacggcacc	gccgccttgc 120
cgccggcaga acttctacaa c	ccccacctc gctc	agaccg gaacgcagcc	aaaggcccc 180
gggccggctc agcgccatac g	tactacagc gagt	gcgacg aatttcgatt	tatcgccccg 240
cgttcgctgg acgaggacgc c	cccgcggag cagc	gcaccg gggtccacga	cggccgcctc 300
cggcgcgccc ctaaggtgta c	tgcgggggg gacg	agegeg aegteeteeg	cgtgggcccg 360
gagggettet ggeegegteg G	ttgcgcctg tggg	gcggtg cggaccatgc	ccccgagggg 420
ttcgacccca ccgtcaccgt c	ttccacgtg tacg	acatcc tggagcacgt	ggaacacgcg 480
tacagcatgc gcgccgccca g	ctccacgag cgat	ttatgg acgccatcac	gcccgccggg 540
accgtcatca cgcttctggg t	ctgaccccc gaag	gccatc gcgtcgccgt	tcacgtctac 600
ggcacgcggc agtactttta c	atgaacaag gcgg	aggtgg atcggcacct	gcagtgccgt 660
gccccgcgcg atctctgcga g	egeetggeg gegg	ccctgc gcgagtcgcc	gggggcgtcg 720
ttccgcggca tctccgcgga c	cacttegag gegg	aggtgg tggagcgcgc	cgacgtgtac 780
tattacgaaa cgcgcccgac c	ctgtactac cgcg	tcttcg tgcgaagcgg	gcgcgcgctg 840
gcctacctgt gcgacaactt t	tgccccgcg atca	ggaagt acgagggggg	cgtcgacgcc 900
accacccggt ttatcctgga c	aacccgggg tttg	tcacct tcggctggta	ccgcctcaag 960
cccggccgcg ggaacgcgcc g	geceaaceg egec	ccccga cggcgttcgg	aacctcgagc 1020
gacgtcgagt ttaactgcac g	geggacaae etgg	ccgtcg agggggccat	gtgtgacctg 1080
ccggcctaca agctcatgtg c	ttcgatatc gaat	gcaagg ccggggggga	ggacgagctg 1140

gcctttccgg	tcgcggaacg	cccggaagac	ctcgtcatcc	agatctcctg	tctgctctac	1200
gacctgtcca	ccaccgccct	cgagcacatc	ctcctgtttt	cgctcggatc	ctgcgacctc	1260
cccgagtccc	acctcagcga	tctcgcctcc	aggggcctgc	cggcccccgt	cgtcctggag	1320
tttgacagcg	aattcgagat	gctgctggcc	ttcatgacct	tcgtcaagca	gtacggcccc	1380
gagttcgtga	ccgggtacaa	catcatcaac	ttcgactggc	ccttcgtcct	gaccaagctg	1440
acggagatct	acaaggtccc	gctcgacggg	tacgggcgca	tgaacggccg	gggtgtgttc	1500
cgcgtgtggg	acatcggcca	gagccacttt	cagaagcgca	gcaagatcaa	ggtgaacggg	1560
atggtgaaca	tcgacatgta	cggcatcatc	accgacaagg	tcaaactctc	cagctacaag	1620
ctgaacgccg	tcgccgaggc	cgtcttgaag	gacaagaaga	aggatctgag	ctaccgcgac	1680
atccccgcct	actacgcctc	cgggcccgcg	cagcgcgggg	tgatcggcga	gtattgtgtg	1740
caggactcgc	tgctggtcgg	gcagctgttc	ttcaagtttc	tgccgcacct	ggagctttcc	1800
gccgtcgcgc	gcctggcggg	catcaacatc	acccgcacca	tctacgacgg	ccagcagatc	1860
cgcgtcttca	cgtgcctcct	gcgccttgcg	ggccagaagg	gcttcatcct	gccggacacc	1920
caggggcggt	ttcggggcct	cgacaaggag	gcgcccaagc	gcccggccgt	gcctcggggg	1980
gaaggggagc	ggccggggga	cgggaacggg	gacgaggata	aggacgacga	cgaggacggg	20,40
gacgaggacg	gggacgagcg	cgaggaggtc	gcgcgcgaga	ccgggggccg	gcacgttggg	2100
taccaggggg	cccgggtcct	cgaccccacc	tccgggtttc	acgtcgaccc	cgtggtggtg	2160
tttgactttg	ccagcctgta	ccccagcatc	atccaggccc	acaacctgtg	cttcagtacg	2220
ctctccctgc	ggcccgaggc	cgtcgcgcac	ctggaggcgg	accgggacta	cctggagatc	2280
gaggtggggg	gccgacggct	gttcttcgtg	aaggcccacg	tacgcgagag	cctgctgagc	2340
atcctgctgc	gcgactggct	ggccatgcga	aagcagatcc	gctcgcggat	ccccagagc	2400
cccccgagg	aggccgtcct	cctcgacaag	caacaggccg	ccatcaaggt	ggtgtgcaac	2460
tcggtgtacg	ggttcaccgg	ggcgcagcac	ggtcttctgc	cctgcctgca	cgtggccgcc	2520
accgtgacga	ccatcggccg	cgagatgctc	ctcgcgacgc	gcgcgtacgt	gcacgcgcgc	2580
tgggcggagt	tcgatcagct	gctggccgac	tttccggagg	cggccggcat	gcgcgccccc	2640
ggtccgtact	ccatgcgcat	catctacggg	gacacggact	ccattttcgt	tttgtgccgc	2700
ggcctcacgg	ccgcgggcct	ggtggccatg	ggcgacaaga	tggcgagcca	catctcgcgc	2760
gcgctgttcc	tcccccgat	caagctcgag	tgcgaaaaaa	cgttcaccaa	gctgctgctc.	2820
atcgccaaga	aaaagtacat	cggcgtcatc	tgcgggggca	agatgctcat	caagggcgtg	2880
gatctggtgc	gcaaaaacaa	ctgcgcgttt	atcaaccgca	cctccagggc	cctggtcgac	2940
ctgctgtttt	acgacgatac	cgtatccgga	gcggccgccg	cgttagccga	gcgccccgca	3000

gaggagtggc	tggcgcgacc	cctgcccgag	ggactgcagg	cgttcggggc	cgtcctcgta	3060
gacgcccatc	ggcgcatcac	cgacccggag	agggacatcc	aggactttgt	cctcaccgcc	3120
gaactgagca	gacacccgcg	cgcgtacacc	aacaagcgcc	tggcccacct	gacggtgtat	3180
tacaagctca	tggcccgccg	cgcgcaggtc	ccgtccatca	aggaccggat	cccgtacgtg	3240
atcgtggccc	agacccgcga	ggtagaggag	acggtcgcgc	ggctggccgc	cctccgcgag	3300
ctagacgccg	ccgccccagg	ggacgagccc	gccccccag	cggccctgcc	ctccccggcc	3360
aagcgccccc	gggagacgcc	gtcgcatgcc	gaccccccgg	gaggcgcgtc	caagccccgc	3420
aagctgctgg	tgtccgagct	ggcggaggat	cccgggtacg	ccatcgcccg	gggcgttccg	3480
ctcaacacgg	actattactt	ctcgcacctg	ctgggggcgg	cctgcgtgac	gttcaaggcc	3540
ctgtttggaa	ataacgccaa	gatcaccgag	agtctgttaa	agaggtttat	tcccgagacg	3600
tggcaccccc	cggacgacgt	ggccgcgcgg	ctcagggccg	cggggttcgg	gccggcgggg	3660
gccggcgcta	cggcggagga	aactcgtcga	atgttgcata	gagcctttga	tactctagca	3720
tga						3723

<sup>&</sup>lt;210> 4

<400> 4

Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala 20 25 30

Thr Gln Thr Ala Pro Pro Pro Cys Arg Arg Gln Asn Phe Tyr Asn Pro 35 40 45

His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln 50 55 60

Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro 65 70 75 80

Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His 85 90 95

Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu 100 105 110

Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu 115 120 125

Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr 130 135 140

Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala

<sup>&</sup>lt;211> 1240

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

145					150					155					160
Tyr	Ser	Met	Arg	Ala 165	Ala	Gln	Leu	His	Glu 170	Arg	Phe	Met	Asp	Ala 175	Ile
Thr	Pro	Ala	Gly 180	Thr	Val	Ile	Thr	Ьеи 185	Leu	Gly	Leu	Thr	Pro 190	Glu	Gly
His	Arg	Val 195	Ala	Val	His	Val	Tyr 200	Gly	Thr	Arg	Gln	Tyr 205	Phe	Tyr	Met
Asn	Lys 210	Ala	Glu	Val	Asp	Arg 215	His	Leu	Gln	Cys	Arg 220	Ala	Pro	Arg	Asp
Leu 225	Суз	Glu	Arg	Leu	Ala 230	Ala	Ala	Leu	Arg	Glu 235	Ser	Pro	Gly	Ala	Ser 240
Phe	Arg	Gly	Ile	Ser 245	Ala	Asp	His	Phe	Glu 250	Ala	Glu	Val	Val	Glu 255	Arg
Ala	Asp	Val	Tyr 260	Tyr	Tyr	Glu	Thr	Arg 265	Pro	Thr	Leu	Tyr	Туr 270	Arg	Val
Phe	Val	Arg 275	Ser	Gly	Arg	Ala	Leu 280	Ala	Tyr	Leu	Cys	Asp 285	Asn	Phe	Cys
Pro	Ala 290	Ile	Arg	Lys	Tyr	Glu 295	Gly	Gly	Val	Asp	Ala 300	Thr	Thr	Arg	Phe
Ile 305	Leu	Asp	Asn	Pro	Gly 310	Phe	Val	Thr	Phe	Gly 315	Trp	Tyr	Arg	Leu	Lys 320
Pro	Gly	Arg	Gly	Asn 325	Ala	Pro	Ala	Gln	Pro 330	Arg	Pro	Pro	Thr	Ala 335	Phe
Gly	Thr	Ser	Ser 340	Asp	Val	Glu	Phe	Asn 345	Cys	Thr	Ala	Asp	Asn 350	Leu	Ala
Val	Glu	Gly 355	Ala	Met	Cys	Asp	Leu 360	Pro	Ala	Tyr	Lys	Leu 365	Met	Cys	Phe
Asp	Ile 370	Glu	Cys	Lys	Ala	Gly 375	Gly	Glu	Asp	Glu	Leu 380	Ala	Phe	Pro	Val
Ala 385	Glu	Arg	Pro	Glu	Asp 390	Leu	Val	Ile	Gln	Ile 395	Ser	Cys	Leu	Leu	Tyr 400
Asp	Leu	Ser	Thr	Thr 405	Ala	Leu	Glu	His	Ile 410	Leu	Leu	Phe	Ser	Leu 415	Gly
Ser	Cys	Asp	Leu 420	Pro	Glu	Ser	His	Leu 425	Ser	Asp	Leu	Ala	Ser 430	Arg	Gly
Leu	Pro	Ala 435	Pro	Val	Val	Leu	Glu 440	Phe	Asp	Ser	Glu	Phe 445	Glu	Met	Leu
Leu	Ala 450	Phe	Met	Thr	Phe	Val 455	Lys	Gln	Tyr	Gly	Pro 460	Glu	Phe	Val	Thr
Gly 465	Tyr	Asn	Ile	Ile	Asn 470	Phe	Asp	Trp	Pro	Phe 475	Val	Leu	Thr	Lys	Leu 480

Thr	Glu	Ile	Tyr	Lys 485	Val	Pro	Leu	Asp	Gly 490	Tyr	Gly	Arg	Met	Asn 495	Gly
Arg	Gly	Val	Phe 500	Arg	Val	Trp	Asp	Ile 505	Gly	Gln	Ser	His	Phe 510	Gln	Lys
Arg	Ser	Lys 515	Ile	Lys	Val	Asn	Gly 520	Met	Val	Asn	Ile	Asp 525	Met	Tyr	Gly
Ile	Ile 530	Thr	Asp	Lys	Val	Lys 535	Leu	Ser	Ser	Tyr	Lys 540	Leu	Asn	Ala	Val
Ala 545	Glu	Ala	Val	Leu	Lys 550	Asp	Lys	Lys	Lys	Asp 555	Leu	.Ser	Tyr	Arg	Asp 560
Ile	Pro	Ala	Tyr	Tyr 565	Ala	Ser	Gly	Pro	Ala 570	Gln	Arg	Gly	Val	Ile 575	Gly
Glu	Tyr	Cys	Val 580	Gln	Asp	Ser	Leu	Leu 585	Val	Gly	Gln	Leu	Phe 590	Phe	Lys
Phe	Leu	Pro 595	Hìs	Leu	Glu	Leu	Ser 600	Ala	Val	Ala	Arg	Leu 605	Ala	Gly	Ile
Asn	Ile 610	Thr	Arg	Thr	Ile	Tyr 615	Asp	Gly	Gln	Gln	Ile 620	Arg	Val	Phe	Thr
Cys 625	Leu	Leu	Arg	Leu	Ala 630	Gly	Gln	Lys	Gly	Phe 635	Ile	Leu	Pro	Asp	Thr 640
Gln	Gly	Arg	Phe	Arg 645	Gly	Leu	Asp	Lys	Glu 650	Ala	Pro	Lys	Arg	Pro 655	Ala
Val	Pro	Arg	Gly 660		Gly	Glu	Arg	Pro 665	Gly	Asp	Gly	Asn	Gly 670	Asp	Glu
Asp	Lys	Asp 675	Asp	Asp	Glu	Asp	Gly 680	Asp	Glu	Asp	Gly	Asp 685	Glu	Arg	Glu
Glu	Val 690	Ala	Arg	Glu	Thr	Gly 695	Gly	Arg	His	Val	Gly 700	Tyr	Gln	Gly	Ala
Arg 705	Val	Leu	Asp	Pro	Thr 710	Ser	Gly	Phe	His	Val 715	Asp	Pro	Val	Val	Val 720
Phe	qaA	Phe	Ala	Ser 725	Leu	Tyr	Pro	Ser	Ile 730	Ile	Gln	Ala	His	Asn 735	Leu
Cys	Phe	Ser	Thr 740	Leu	Ser	Leu	Arg	Pro 745	Glu	Ala	Val	Ala	His 750	Leu	Glu
Ala	Asp	Arg 755	Asp	Tyr	Leu	Glu	Ile 760	Glu	Val	Gly	Gly	Arg 765	Arg	Leu	Phe
Phe	Val 770	Lys	Ala	His	Va1	Arg 775	Glu	Ser	Leu	Leu	Ser 780	Ile	Leu	Leu	Arg
Asp 785	Trp	Leu	Ala	Met	Arg 790	Lys	Gln	Ile	Arg	Ser 795	Arg	Ile	Pro	Gln	Ser 800
Pro	Pro	Glu	Glu	Ala 805	Val	Leu	Leu	Asp	Lys 810	Gln	Gln	Ala	Ala	Ile 815	Lys

Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu 820 825 Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu 840 Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe 855 Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe 890 Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys 920 Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val 950 955 Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His 1015 1020 Arg Arg Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu 1025 1030 1035 Thr Ala Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg 1045 1.050 Leu Ala His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala 1055 1060 1065 Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala 1070 1075 1080 Gln Thr Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu 1085 1090 Arg Glu Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro 1100 1105 1110 Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser 1120 1125 His Ala Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu

1130	1135	1140
Val Ser Glu Leu Ala Glu 1145	Asp Pro Gly Tyr Al 1150	la Ile Ala Arg Gly 1155
Val Pro Leu Asn Thr Asp 1160	Tyr Tyr Phe Ser Hi 1165	is Leu Leu Gly Ala 1170
Ala Cys Val Thr Phe Lys	Ala Leu Phe Gly As 1180	sn Asn Ala Lys Ile 1185
Thr Glu Ser Leu Leu Lys 1190	Arg Phe Ile Pro Gl 1195	lu Thr Trp His Pro 1200
Pro Asp Asp Val Ala Ala 1205	Arg Leu Arg Ala Al 1210	ia Gly Phe Gly Pro 1215
Ala Gly Ala Gly Ala Thr 1220	Ala Glu Glu Thr Ar 1225	rg Arg Met Leu His 1230
Arg Ala Phe Asp Thr Leu 1235	1 Ala 1240	
<210> 5 <211> 3708 <212> DNA <213> herpes simplex		
<400> 5		
atgttttccg gtggcggcgg cc	ecgetgtee eeeggaggaa	agtcggcggc cagggcggcg 60
tccgggtttt ttgcgcccgc cg	gccctcgc ggagccggcc	ggggaccccc gccttgtttg 120
aggcaaaact tttacaaccc ct	acctcgcc ccagtcggga	cgcaacagaa gccgaccggg 180
ccaacccagc gccatacgta ct	atagcgaa tgcgatgaat	ttcgattcat cgccccgcgg 240
gtgctggacg aggatgcccc co	ecggagaag cgcgccgggg	tgcacgacgg tcacctcaag 300
cgcgcccca aggtgtactg cg	ggggggac gagcgcgacg	tcctccgcgt cgggtcgggc 360
ggettetgge egeggegete ge	gcctgtgg ggcggcgtgg	accacgcccc ggcggggttc 420
aaccccaccg tcaccgtctt to	acgtgtac gacatcctgg	agaacgtgga gcacgcgtac 480
ggcatgcgcg cggcccagtt co	acgcgcgg tttatggacg	ccatcacacc gacggggacc 540
gtcatcacgc teetgggeet ga	ctccggaa ggccaccggg	tggccgttca cgtttacggc 600
acgcggcagt acttttacat ga	acaaggag gaggttgaca	ggcacctaca atgccgcgcc 660
ccacgagatc tctgcgagcg ca	tggccgcg gccctgcgcg	agtccccggg cgcgtcgttc 720
cgcggcatct ccgcggacca ct	tcgaggcg gaggtggtgg	agegeacega egtgtactae 780
tacgagacgc gccccgctct gt	tttaccgc gtctacgtcc	gaagcgggcg cgtgctgtcg 840
tacctgtgcg acaacttctg co	cggccatc aagaagtacg	agggtggggt cgacgccacc 900
acceggttca teetggacaa co	ccgggttc gtcaccttcg	gctggtaccg tctcaaaccg 960
ggccggaaca acacgctagc co	agccgcgg gccccgatgg	ccttcgggac atccagcgac 1020

gtcgagttta	actgtacggc	ggacaacctg	gccatcgagg	ggggcatgag	cgacctaccg	1080
gcatacaagc	tcatgtgctt	cgatatcgaa	tgcaaggcgg	ggggggagga	cgagctggcc	1140
tttccggtgg	ccgggcaccc	ggaggacctg	gttattcaga	tatcctgtct	gctctacgac	1200
ctgtccacca	ccgccctgga	gcacgtcctc	ctgttttcgc	tcggttcctg	cgacctcccc	1260
gaatcccacc	tgaacgagct	ggcggccagg	ggcctgccca	cgcccgtggt	tctggaattc	1320
gacagcgaat	tcgagatgct	gttggccttc	atgacccttg	tgaaacagta	cggccccgag	1380
ttcgtgaccg	ggtacaacat	catcaacttc	gactggccct	tcttgctggc	caagttgacg	1440
gacatttaca	aggtccccct	ggacgggtac	ggccgcatga	acggccgggg	cgtgtttcgc	1500
gtgtgggaca	taggccagag	ccacttccag	aagcgcagca	agataaaggt	gaacggcatg	1560
gtgaacatcg	acatgtacgg	gatcataacc	gacaagatca	agctctcgag	ctacaagctc	1620
aacgccgtgg	ccgaagccgt	cctgaaggac	aagaagaagg	acctgagcta	tcgcgacatc	1680
cccgcctact	acgccgccgg	gcccgcgcaa	cgcggggtga	tcggcgagta	ctgcatacag	1740
gattccctgc	tggtgggcca	gctgttttt	aagtttttgc	cccatctgga	gctctcggcc	1800
gtcgcgcgct	tggcgggtat	taacatcacc	cgcaccatct	acgacggcca	gcagatccgc	1860
gtctttacgt	gcctgctgcg	cctggccgac	cagaagggct	ttattctgcc	ggacacccag	1920
gggcgattta	ggggcgccgg	gggggaggcg	cccaagcgtc	cggccgcagc	ccgggaggac	1980
gaggagcggc	cagaggagga	gggggaggac	gaggacgaac	gcgaggaggg	cgggggcgag	2040
cgggagccgg	agggcgcgcg	ggagaccgcc	ggccggcacg	tggggtacca	gggggccagg	2100
gtccttgacc	ccacttccgg	gtttcacgtg	aaccccgtgg	tggtgttcga	ctttgccagc	2160
ctgtacccca	gcatcatcca	ggcccacaac	ctgtgcttca	gcacgctctc	cctgagggcc	2220
gacgcagtgg	cgcacctgga	ggcgggcaag	gactacctgg	agatcgaggt	gggggggcga	2280
cggctgttct	tcgtcaaggc	tcacgtgcga	gagagcctcc	tcagcatcct	cctgcgggac	2340
tggctcgcca	tgcgaaagca	gatccgctcg	cggattcccc	agagcagccc	cgaggaggcc	2400
gtgctcctgg	acaagcagca	ggccgccatc	aaggtcgtgt	gtaactcggt	gtacgggttc	2460
acgggagcgc	agcacggact	cctgccgtgc	ctgcacgttg	ccgcgacggt	gacgaccatc	2520
ggccgcgaga	tgctgctcgc	gacccgcgag	tacgtccacg	cgcgctgggc	ggccttcgaa	2580
cagctcctgg	ccgatttccc	ggaggcggcc	gacatgegeg	ccccgggcc	ctattccatg	2640
cgcatcatct	acggggacac	ggactccata	tttgtgctgt	gccgcggcct	cacggccgcc	2700
gggctgacgg	ccatgggcga	caagatggcg	agccacatct	cgcgcgcgct	gtttctgccc	2760
cccatcaaac	tcgagtgcga	aaagacgttc	accaagetge	tgctgatcgc	caagaaaaag	2820
tacatcggcg	tcatctacgg	gggtaagatg	ctcatcaagg	gcgtggatct	ggtgcgcaaa	2880

aacaactgcg	cgtttatcaa	ccgcacctcc	agggccctgg	tcgacctgct	gttttacgac	2940
gataccgtat	ccggagcggc	cgccgcgtta	gccgagcgcc	ccgcagagga	gtggctggcg	3000
cgacccctgc	ccgagggact	gcaggcgttc	ggggccgtcc	tcgtagacgc	ccatcggcgc	3060
atcaccgacc	cggagaggga	catccaggac	tttgtcctca	ccgccgaact	gagcagacac	3120
ccgcgcgcgt	acaccaacaa	gcgcctggcc	cacctgacgg	tgtattacaa	gctcatggcc	3180
egcegegege	aggtcccgtc	catcaaggac	cggatcccgt	acgtgatcgt	ggcccagacc	3240
cgcgaggtag	aggagacggt	cgcgcggctg	gccgccctcc	gcgagctaga	cgccgccgcc	3300
ccaggggacg	agcccgcccc	ccccgcggcc	ctgccctccc	cggccaagcg	ccccgggag	3360
acgccgtcgc	atgccgaccc	cccgggaggc	gcgtccaagc	cccgcaagct	gctggtgtcc	3420
gagctggccg	aggatecege	atacgccatt	gcccacggcg	tcgccctgaa	cacggactat	3480
tacttctccc	acctgttggg	ggcggcgtgc	gtgacattca	aggccctgtt	tgggaataac	3540
gccaagatca	ccgagagtct	gttaaaaagg	tttattcccg	aagtgtggca	cccccggac	3600
gacgtggccg	cgcggctccg	ggccgcaggg	ttcggggcgg	tgggtgccgg	cgctacggcg	3660
gaggaaactc	gtcgaatgtt	gcatagagcc	tttgatactc	tagcatga		3708

<sup>&</sup>lt;210> 6

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg 115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val

<sup>&</sup>lt;211> 1235

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

<sup>&</sup>lt;400> 6

135 140 130 Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr 155 150 Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr 170 Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His 185 Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe 235 230 Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr 250 Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr 265 Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile 345 Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp 360 Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala 375 Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp 390 395 Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly

455

16

Tyr 465	Asn	Ile	Ile	Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480
Asp	Ile	Tyr	Lys	Val 485	Pro	Leu	Asp	Gly	Туr 490	Gly	Arg	Met	Asn	Gly 495	Arg
Gly	Val	Phe	Arg 500	Val	Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg
Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile	Thr 530	Asp	Lys	Ile	Lys	Leu 535	Ser	Ser	Tyr	Lys	Leu 540	Asn	Ala	Val	Ala
545	Ala				550					555					560
Pro	Ala	Tyr	Tyr	Ala 565	Ala	Gly	Pro	Ala	Gln 570	Arg	Gly	Val	Ile	Gly 575	Glu
Tyr	Cys	Ile	Gln 580	Asp	Ser	Leu	Leu	Val 585	Gly	Gln	Leu	Phe	Phe 590	Lys	Phe
Leu	Pro	His 595	Leu	Glu	Leu	Ser	Ala 600	Val	Ala	Arg	Leu	Ala 605	Gly	Ile	Asn
	Thr 610	_			_	615					620				_
625	Leu				630					635					640
	Arg			645					650					655	
	Arg		660			_		665					670		_
	Arg	675					680					685			
	Ala 690					695				3	700			. •	•
705	Ser	<del></del>			710					715					720
	Tyr			725		_			730		_			735	
	Leu		740					745					750	_	
	Glu	755					760					765			
	Arg 770					775					780				
Arg 785	Lys	GIn	I1e	Arg	Ser 790	Arg	ITE	Pro	GIn	Ser 795	Ser	Pro	GLu	Glu	Ala 800

Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Ala Gln His Gly Leu Leu Pro Cys Leu His 825 Val Ala Ala Thr Val Thr Ile Gly Arg Glu Met Leu Leu Ala Thr 840 Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met 870 875 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly 890 Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His 905 Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val 935 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln 1000 Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp 1020 1010 1015 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser 1025 1030 1035 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr 1040 1045 1050 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile 1055 1060 1065 Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val 1075 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala 1085 1090 1095 Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser 1105 Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala Asp Pro Pro

1	1115					1120					1125				
	31y .130	Ala	Ser	Lys	Pro	Arg 1135	Lys	Leu	Leu	Val	Ser 1140	Glu	Leu	Ala	
	Asp .145	Pro	Ala	Tyr	Ala	Ile 1150	Ala	His	Gly	Val	Ala 1155	Leu	Asn	Thr	
	Tyr 1160	Tyr	Phe	Ser	His	Leu 1165	Leu	Gly	Ala	Ala	Cys 1170	Val	Thr	Phe	
-	Ala 175	Leu	Phe	Gly	Asn	Asn 1180	Ala	Lys	Ile	Thr	Glu 1185	Ser	Leu	Leu	
_	Arg 1190	Phe	Ile	Pro	Glu	Val 1195	Trp	His	Pro	Pro	Asp 1200	Asp	Val	Ala	
Ala A 1	Arg 1205	Leu	Arg	Ala	Ala	Gly 1210	Phe	Gly	Ala	Val	Gly 1215	Ala	Gly	Ala	
	Ala 1220	Glu	Glu	Thr	Arg	Arg 1225	Met	Leu	His	Arg	Ala 1230	Phe	Asp	Thr	
Leu A	Ala 1235														
<210><211><212><213>	> 37 > DN	Α	s sin	nplex	5										
<400> atgtt		g gt	ggcg	ggcgg	l cc	egetgt	ccc o	cccgg	gagga	aa ag	gtcggo	egge	cagg	igcggcg	60
tccgg	gttt	t tt	gcgc	ccgc	: cgg	gcccto	gc g	ggago	ccggc	cc gg	gggac	ccc	gaat	tgcttg	120
aggca	aaaac	t tt	taca	acco	cta	acctc	gcc (	ccagt	cggg	ja c	gcaaca	agaa	gccg	accggg	180
ccaac	ccag	c go	ccata	acgta	ı cta	atagco	gaa t	tgcga	atgaa	at ti	tcgati	cat	cgcc	ccgcgg	240
gtgct	ggac	g ag	ggato	jecec	ccc	ggaga	aag d	cgcgo	ccggo	gg to	gcacga	acgg	tcac	ctcaag	300
cgcgc	cccc	a ag	ggtgt	acto	ı cgg	agagg	gac g	gagco	gcgaç	g to	cctcc	gcgt	cggg	ıtcgggc	360
ggctt	ctgg	c cg	gegge	egete	gcg	gcctgt	ag s	ggcgg	: gagtg	gg a	ccacgo	ccc	ggcg	gggttc	420
aaccc	ccacc	g to	cacco	gtctt	tca	acgtgt	cac g	gacat	cctg	gg ag	gaacgi	gga	gcac	gcgtac	480
ggcat	gege	a cc	ggccc	cagtt	. cca	acgcgo	cgg t	tttat	ggad	eg co	catcad	cacc	gaco	gggacc	540
gtcat	cacg	c to	cctgg	ggaat	gac	ctccgg	gaa g	ggcca	accgg	gg to	ggccgt	tca	cgtt	tacggc	600
acgcg	gcag	t ac	etttt	acat	gaa	acaagg	gag g	gaggt	cgao	ca g	gcacci	caca	atgo	cgcgcc	660
ccacg	gagat	c to	ctgcg	gagco	, cat	ggcc	gcg g	gacat	gege	g a	gtccc	ggg	cgcg	stegtte	720
cgcgg	gcatt	t co	gegg	gacca	ctt	cgag	geg g	gaggt	ggtg	gg a	gcgcad	ccga	cgts	tactac	780
tacga	agacg	c go	cccc	gctct	gtt	ttaco	ege g	gtcta	acgto	cc ga	aagcg	ggcg	cgts	ctgtcg	840
tacct	gtgç	g ac	caact	tctc	ı cc	ggcca	atc a	aagaa	agtac	g ag	gggtgg	gggt	cgac	gccacc	900

acccggttca t	tcctggacaa	ccccgggttc	gtcaccttcg	gctggtaccg	tctcaaaccg	960
ggccggaaca a	acacgctagc	ccagccgcgg	gccccgatgg	ccttcgggac	atccagcgac	1020
gtcgagttta a	actgtacggc	ggacaacctg	gccatcgagg	ggggcatgag	cgacctaccg	1080
gcatacaagc t	catgtgctt	cgatatcgaa	tgcaaggcgg	ggggggagga	cgagctggcc	1140
tttccggtgg o	cgggcaccc	ggaggacctg	gtcatccaga	tatcctgtct	gctctacgac	1200
ctgtccacca c	ccgccctgga	gcacgtcctc	ctgttttcgc	teggtteetg	cgacctcccc	1260
gaatcccacc t	tgaacgagct	ggcggccagg	ggcctgccca	cgcccgtggt	tctggaattc	1320
gacagcgaat t	cgagatgct	gttggccttc	atgacccttg	tgaaacagta	cggccccgag	1380
ttcgtgaccg g	ggtacaacat	catcaacttc	gactggccct	tcttgctggc	caagctgacg	1440
gacatttaca a	aggtccccct	ggacgggtac	ggccgcatga	acggccgggg	cgtgtttcgc	1500
gtgtgggaca t	caggccagag	ccacttccag	aagcgcagca	agataaaggt	gaacggcatg	1560
gtgaacatcg a	acatgtacgg	gattataacc	gacaagatca	agctctcgag	ctacaagctc	1620
aacgccgtgg d	ccgaagccgt	cctgaaggac	aagaagaagg	acctgagcta	tcgcgacatc	1680
cccgcctact a	acgccgccgg	gcccgcgcaa	cgcggggtga	tcggcgagta	ctgcatacag	1740
gattccctgc t	ggtgggcca	gctgttttt	aagtttttgc	cccatctgga	gctctcggcc	1800
gtcgcgcgct t	ggcgggtat	taacatcacc	cgcaccatct	acgacggcca	gcagatccgc	1860
gtctttacgt g	geetgetgeg	cctggccgac	cagaagggct	ttattctgcc	ggacacccag	1920
gggcgattta g	gggcggcgg	gggggaggcg	cccaagcgtc	cggccgcagc	ccgggaggac	1980
gaggagegge o	cagaggagga	gggggaggac	gaggacgaac	gcgaggaggg	cgggggcgag	2040
cgggagccgg a	agggcgcgcg	ggagaccgcc	ggccggcacg	tggggtacca	gggggccagg	2100
gtccttgacc c	ccacttccgg	gtttcatgtg	aaccccgtgg	tggtgttcga	ctttgccagc	2160
ctgtacccca g	gcatcatcca	ggcccacaac	ctgtgcttca	gcacgctctc	cctgagggcc	2220
gacgcagtgg c	egcacctgga	ggcgggcaag	gactacctgg	agatcgaggt	gggggggcga	2280
cggctgttct t	cgtcaaggc	tcacgtgcga	gagagcctcc	tcagcatcct	cctgcgggac	2340
tggctcgcca t	gcgaaagca	gatccgctcg	cggattcccc	agagcagccc	cgaggaggcc	2400
gtgctcctgg a	acaagcagca	ggccgccatc	aaggtcgtgt	gtaactcggt	ttacgggttc	2460
acgggagcgc a	agcacggact	cctgccgtgc	ctgcacgttg	ccgcgacggt	gacgaccatc	2520
ggccgcgaga t	getgetege	gacccgcgag	tacgtccacg	cgcgctgggc	ggccttcgaa	2580
cagctcctgg c	cgatttccc	ggaggcggcc	gacatgcgcg	ccccgggcc	ctattccatg	2640
cgcatcatct a	acggggacac	ggactccatc	tttgtgctgt	gccgcggcct	cacggccgcc	2700
gggctgacgg c	cgtgggcga	caagatggcg	agccacatct	cgcgcgcgct	gtttctgtcc	2760

cccatcaaac	tcgagtgcga	aaagacgttc	accaagctgc	tgctgatcgc	caagaaaaag	2820
tacatcggcg	tcatctacgg	gggtaagatg	ctcatcaagg	gcgtggatct	ggtgcgcaaa	2880
aacaactgcg	cgtttatcaa	ccgcacctcc	agggccctgg	tcgacctgct	gttttacgac	2940
gataccgtat	ccggagcggc	cgccgcgtta	gccgagcgcc	ccgcagagga	gtggctggcg	3000
cgacccctgc	ccgagggact	gcaggcgttc	ggggccgtcc	tcgtagacgc	ccatcggcgc	3060
atcaccgacc	cggagaggga	catccaggac	tttgtcctca	ccgccgaact	gagcagacac	3120
ccgcgcgcgt	acaccaacaa	gcgcctggcc	cacctgacgg	tgtattacaa	gctcatggcc	3180
cgccgcgcgc	aggtcccgtc	catcaaggac	cggatcccgt	acgtgatcgt	ggcccagacc	3240
cgcgaggtag	aggagacggt	cgcgcggctg	gccgccctcc	gcgagctcga	cgccgccgcc	3300
ccaggggacg	agcccgcccc	cccgcggcc	ctgccctccc	cggccaagcg	ccccgggag	3360
acgccgttgc	atgccgaccc	cccgggaggc	gcgtccaagc	cccgcaagct	gctggtgtcc	3420
gagctggccg	aggatecege	atacgccatt	gcccacggcg	tcgccctgaa	cacggactat	3480
tacttctccc	acctgttggg	ggcggcgtgc	gtgacattca	aggccctgtt	tgggaataac	3540
gccaagatca	ccgagagtct	gttaaaaagg	tttattcccg	aagtgtggca	cccccggac	3600
gacgtggccg	cgcggctccg	ggccgcaggg	ttcggggcgg	tgggtgccgg	cgctacggcg	3660
gaggaaactc	gtcgaatgtt	gcatagagcc	tttgatactc	tagcatga		3708

<sup>&</sup>lt;210> 8

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 7.0 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg

<sup>&</sup>lt;211> 1235

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

<sup>&</sup>lt;400> 8

115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val 1.35 140 Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr 155 Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His 185 Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu 215 220 Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe 230 Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr 245 250 Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro 280 Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp 385 390 395 Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser 405 410 Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu 425 Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu 435 445 440

Ala	Phe 450	Met	Thr	Leu	Val	Lys 455	Gln	Tyr	Gly	Pro	Glu 460	Phe	Val	Thr	Gly
Tyr 465	Asn	Ile	Ile	Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480
Asp	Ile	Tyr	Lys	Val 485	Pro	Leu	Asp	Gly	Tyr 490	Gly	Arg	Met	Asn	Gly 495	Arg
Gly	Val	Phe	Arg 500	Val	Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg
Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile	Thr 530	Asp	Lys	Ile	Lys	Leu 535	Ser	Ser	Tyr	Lys	Leu 540	Asn	Ala	Val	Ala
Glu 545	Ala	Val	Leu	Lys	Asp 550	Lys	Lys	Lys	Asp	Leu 555	Ser	Tyr	Arg	Asp	Ile 560
Pro	Ala	Tyr	Tyr	Ala 565	Ala	Gly	Pro	Ala	Gln 570	Arg	Gly	Val	Ile	Gly 575	Glu
Tyr	Cys	Ile	Gln 580	Asp	Ser	Leu	Leu	Val 585	Gly	Gln	Leu	Phe	Phe 590	Lys	Phe
Leu	Pro	His 595	Leu	Glu	Leu	Ser	Ala 600	Val	Ala	Arg	Leu	Ala 605	Gly	Ile	Asn
Ile	Thr 610	Arg	Thr	Ile	Tyr	Asp 615	Gly	Gln	Gln	Ile	Arg 620	Val	Phe	Thr	Cys
Leu 625	Leu	Arg	Leu	Ala	Asp 630	Gln	Lys	Gly	Phe	Ile 635	Leu	Pro	Asp	Thr	Gln 640
Gly	Arg	Phe	Arg	Gly 645	Gly	Gly	Gly	Glu	Ala 650	Pro	Lys	Arg	Pro	Ala 655	Ala
Ala	Arg	Glu	Asp 660	Glu	Glu	Arg	Pro	Glu 665	Glu	Glu	Gly	Glu	Asp 670	Glu	Asp
Glu	Arg	Glu 675	Glu	Gly	Gly	Gly	Glu 680	Arg	Glu	Pro	Glu	Gly 685	Ala	Arg	Glu
Thr	Ala 690	Gly	Arg	His	Val	Gly 695	Tyr	Gln	Gly	Ala	Arg 700	Val	Leu	Asp	Pro
Thr 705	Ser	Gly	Phe	His	Val 710	Asn	Pro	Val	Val	Val 715	Phe	Asp	Phe	Ala	Ser 720
Leu	Tyr	Pro	Ser	Ile 725	Ile	Gln	Ala	His	Asn 730	Leu	Cys	Phe	Ser	Thr 735	Leu
Ser	Leu	Arg	Ala 740	Asp	Ala	Val	Ala	His 745	Leu	Glu	Ala	Gly	Lys 750	Asp	Tyr
Leu	Glu	I1e 755	Glu	Val	Gly	Gly	Arg 760	Arg	Leu	Phe	Phe	Val 765	Lys	Ala	His
Val	Arg 770	Glu	Ser	Leu	Leu	Ser 775	Ile	Leu	Leu	Arg	Asp 780	Trp	Leu	Ala	Met

Arg 785	Lys	Gln	Ile	Arg	Ser 790	Arg	Ile	Pro	Gln	Ser 795	Ser	Pro	Glu	Glu	Ala 800
Val	Leu	Leu	Asp	Lys 805	Gln	Gln	Ala	Ala	Ile 810	Lys	Val	Val	Суѕ	Asn 815	Ser
Val	Tyr	Gly	Phe 820	Thr	Gly	Ala	Gln	His 825	Gly	Leu	Leu	Pro	Суs 830	Leu	His
Va1	Ala	Ala 835	Thr	Val	Thr	Thr	Ile 840	Gly	Arg	Glu	Met	Leu 845	Leu	Ala	Thr
Arg	Glu 850	Tyr	Val	His	Ala	Arg 855	Trp	Ala	Ala	Phe	Glu 860	Gln	Leu	Leu	Ala
Asp 865	Phe	Pro	Glu	Ala	Ala 870	Asp	Met	Arg	Ala	Pro 875	Gly	Pro	Tyr	Ser	Met 880
Arg	Ile	Ile	Tyr	Gly 885	Asp	Thr	Asp	Ser	Ile 890	Phe	Val	Leu	Cys	Arg 895	Gly
Leu	Thr	Ala	Ala 900	Gly	Leu	Thr	Ala	Val 905	Gly	Asp	Lys	Met	Ala 910	Ser	His
Ile	Ser	Arg 915	Ala	Leu	Phe	Leu	Ser 920	Pro	Ile	Lys	Leu	Glu 925	Cys	Glu	Lys
Thr	Phe 930	Thr	Lys	Leu	Leu	Leu 935	Ile	Ala	Lys	Lys	Lys 940	Tyr	Ile	Gly	Val
Ile 945	Tyr	Gly	Gly	Lys	Met 950	Leu	Ile	Lys	Gly	Val 955	Asp	Leu	Val	Arg	Lys 960
Asn	Asn	Cys	Ala	Phe 965	Ile	Asn	Arg	Thr	Ser 970	Arg	Ala	Leu	Val	Asp 975	Leu
Leu	Phe	Tyr	Asp 980	Asp	Thr	Val	Ser	Gly 985	Ala	Ala	Ala	Ala	Leu 990	Ala	Glu
Arg	Pro	Ala 995	Glu	Glu	Trp	Leu	Ala 100		g Pro	) Let	ı Pro	10		ly L	eu Gln
Ala	Phe 1010		y Ala	a Val	. Lev	Val 101		A qu	la`H:	is A		cg : 020	Ile '	Thr I	Asp
Pro	Glu 1025		g Asp	) Ile	e Gln	Asp 103		ne Va	al Le	∋u Tl		La ( )35	Glu 1	Leu :	Ser
Arg	His 1040		Arg	g Ala	туг	Th:		sn Ly	ys Ai	rg Le		La 1 050	His 1	Leu '	Thr
Val	Tyr 1055		. Lys	s Leu	ı Met	Ala 106		rg A	rg A	la G		al :	Pro ;	Ser :	Ile
Lys	Asp 1070		g Il€	e Pro	туг	Val		le Va	al A	la G		nr . 080	Arg (	3lu '	Val
Glu	Glu 1085		· Val	l Ala	a Arg	Let 109		la A	la L	eu Ai		lu : 095	Leu Z	Asp /	Ala
Ala	Ala	Pro	o Gla	, Asr	Glu	Pro	5 A	la P	ro Pi	ro A	la A	la :	Leu :	Pro	Ser

	1100					1105					1110				
Pro	Ala 1115	Lys	Arg	Pro	Arg	Glu 1120	Thr	Pro	Leu	His	Ala 1125	Asp	Pro	Pro	
Gly	Gly 1130	Ala	Ser	Lys	Pro	Arg 1135	Lys	Leu	Leu	Val	Ser 1140	Glu	Leu	Ala	
Glu	Asp 1145	Pro	Ala	Tyr	Ala	Ile 1150	Ala	His	Gly	Val	Ala 1155	Leu	Asn	Thr	
Asp	Tyr 1160	Tyr	Phe	Ser	His	Leu 1165	Leu	Gly	Ala	Ala	Cys 1170	Val	Thr	Phe	
Lys	Ala 1175	Leu	Phe	Gly	Asn	Asn 1180	Ala	Lys	Ile	Thr	Glu 1185	Ser	Leu	Leu	
Lys	Arg 1190	Phe	Ile	Pro	Glu	Val 1195	Trp	His	Pro	Pro	Asp 1200	Asp	Val	Ala	
Ala	Arg 1205	Leu	Arg	Ala	Ala	Gly 1210	Phe	Gly	Ala	Val	Gly 1215	Ala	Gly	Ala	
Thr	Ala 1220	Glu	Glu	Thr	Arg	Arg 1225	Met	Leu	His	Arg	Ala 1230	Phe	Asp	Thr	
Leu	Ala 1235														
		IA.	s sin	mplex	ζ										
<400 atgt		cg gt	ggcg	ggcgg	g cco	egetgt	cee o	cccgg	gagga	aa ag	gteggo	egge	cago	ıgcggcg	60
tccg	ggttt	t tt	gege	cccg	c cgg	geeete	ege g	ggago	ccggo	cc gg	gggac	cccc	gcct	tgtttg	120
aggo	caaaac	et ti	taca	aacco	c cta	acctc	gcc (	ccagt	cggg	ga c	gcaaca	agaa	gccg	gaccggg	180
ccaa	acccaç	gc go	ccata	acgta	a cta	atagco	gaa 1	tgcga	atgaa	at t	tcgati	tcat	cgc	ccgcgg	240
gtgo	ctggad	cg ag	ggato	gece	c cc	ggaga	aag d	cgcgo	ccggg	gg t	gcacga	acgg	tcad	ctcaag	300
cgcg	geeee	ca ag	ggtgt	tacto	g cgg	33333	gac g	gagc	gcgad	cg to	cctcc	gcgt	cggg	ıtcgggc	360
ggct	tctgg	၂၀ င	gegge	egete	e geg	gcctgt	gg g	ggcgg	gcgtg	gg a	ccacgo	ccc	ggcg	gggttc	420
aaco	ccaco	g to	cacco	gtctt	tca	acgtgt	at q	gacat	ccto	gg ag	gaacgt	tgga	gcad	gcgtac	480
ggca	tgcgc	eg eg	ggcco	cagt	c cca	acgcgo	egg t	tttat	ggad	eg co	catcad	cacc	gac	ıgggacc	540
gtca	atcaco	gc to	cctgg	ggcct	gad	ctccgg	gaa g	ggcca	accgg	gg t	ggccgt	ttca	cgtt	tacggc	600
acgo	eggcag	gt ac	ctttt	cacat	c gaa	acaag	gag g	gaggt	tgad	ca g	gcacct	taca	atgo	egegee	660
ccac	gagat	c to	ctgcg	gagcg	g cat	ggccg	geg g	gacat	gege	cg ag	gtece	ggg	cgcg	tcgttc	720
cgcg	gcato	ct co	gegg	gacca	a ctt	cgagg	gcg (	gaggt	tggtg	gg a	gcgcad	ccga	cgtg	gtactac	780
tacc	racacc	יר מי	יכככ	retet	at t	ttacc	מכ נ	atota	acata	-c a	33000	raca	cata	retatea	840

tacctgtgcg	acaacttctg	cccggccatc	aagaagtacg	agggtggggt	cgacgccacc	900
acceggttca	tcctggacaa	ccccgggttc	gtcaccttcg	gctggtaccg	tctcaaaccg	960
ggccggaaca	acacgctagc	ccagccgcgg	gccccgatgg	ccttcgggac	atccagcgat	1020
gtcgagttta	actgtacggc	ggacaacctg	gccatcgagg	ggggcatgag	cgacctaccg	1080
gcatacaagc	tcatgtgctt	cgatatcgaa	tgcaaggcgg	ggggggagga	cgagctggcc	1140
tttccggtgg	ccgggcaccc	ggaggacctg	gtcatccaga	tatcctgtct	gctctacgac	1200
ctgtccacca	ccgccctgga	gcacgtcctc	ctgttttcgc	teggtteetg	cgacctcccc	1260
gaatcccacc	tgaacgagct	ggcggccagg	ggcctgccca	cgcccgtggt	tctggaattc	1320
gacagcgaat	tcgagatgct	gttggccttc	atgacccttg	tgaaacagta	cggccccgag	1380
ttcgtgaccg	ggtacaacat	aatcaacttc	gactggccct	tcttgctggc	caagctgacg	1440
gacatttaca	aggtccccct	ggacgggtac	ggccgcatga	acggccgggg	cgtgtttcgc	1500
gtgtgggaca	taggccagag	ccacttccag	aagcgcagca	agataaaggt	gaacggcatg	1560
gtgaacatcg	acatgtacgg	gattataacc	gacaagatca	agctctcgag	ctacaagctc	1620
aacgccgtgg	ccgaagccgt	cctgaaggac	aagaagaagg	acctgagcta	tcgcgacatc	1680
cccacctact	acgccgccgg	gcccgcgcaa	cgcggggtga	tcggcgagta.	ctgcatacag	1740
gattccctgc	tggtgggcca	gctgttttt	aagtttttgc	cccatctgga	geteteggee	1800
gtcgcgcgct	tggcgggtat	taacatcacc	cgcaccatct	acgacggcca	gcagatccgc	1860
gtctttacgt	gcctgctgcg	cctggccgac	cagaagggct	ttattctgcc	ggacacccag	1920
gggcgattta	ggggcgccgg	gggggaggcg	cccaagcgtc	cggccgcagc	ccgggaggac	1980
gaggagcggc	cagaggagga	gggggaggac	gagaacgaac	gcgaggaggg	cgggggcgag	2040
cgggagccgg	agggcgcgcg	ggagaccgcc	ggccggcacg	tggggtacca	gggggccagg	2100
gtccttgacc	ccacttccgg	gtttcacgtg	aaccccgtgg	tggtgttcga	ctttgccagc	2160
ctgtacccca	gcatcatcca	ggcccacaac	ctgtgcttca	gcacgctctc	cctgagggcc	2220
gacgcagtgg	cgcacctgga	ggcgggcaag	gactacctgg	agatcgaggt	gggggggcga	2280
cggctgttct	tcgtcaaggc	tcacgtgcga	gagagcctcc	tcagcatcct	cctgcgggac	2340
tggctcgcca	tgcgaaagca	gatccgctcg	cggattcccc	agagcagccc	cgaggaggcc	2400
gtgctcctgg	acaagcagca	ggccgccatc	aaggtcgtgt	gtaactcggt	ttacgggttc	2460
acgggagcgc	agcacggact	cctgccgtgc	ctgcacgttg	ccgcgacggt	gacgaccatc	2520
ggccgcgaga	tgctgctcgc	gacccgcgag	tacgtccacg	cgcgctgggc	ggccttcgaa	2580
cageteetgg	ccgatttccc	ggaggcggcç	gacatgcgcg	ccccgggcc	ctattccatg	2640
cgcatcatct	acggggacac	ggactccata	tttgtgctgt	gccgcggcct	cacggccgcc	2700

gggctgacgg	ccgtgggcga	caagatggcg	agccacatct	cgcgcgcgct	gtttctgccc	2760
cccatcaaac	tcgagtgcga	aaagacgttc	accaagctgc	tgctgatcgc	caagaaaaag	2820
tacatcggcg	tcatctacgg	gggtaagatg	ctcatcaagg	gcgtggatct	ggtgcgcaaa	2880
aacaactgcg	cgtttatcaa	ccgcacctcc	agggccctgg	tcgacctgct	gttttacgac	2940
gataccgtat	ccggagcggc	cgccgcgtta	gccgagcgcc	ccgcagagga	gtggctggcg	3000
cgacccctgc	ccgagggact	gcaggcgttc	ggggccgtcc	tcgtagacgc	ccateggege	3060
atcaccgacc	cggagaggga	catccaggac	tttgttctca	ccgccgaact	gagcagacac	3120
ccgcgcgcgt	acaccaacaa	gcgcctggcc	cacctgacgg	tgtattacaa	gctcatggcc	3180
cgccgcgcgc	aggtcccgtc	catcaaggac	cggatcccgt	acgtgatcgt	ggcccagacc	3240
cgcgaggtag	aggagacggt	cgcgcggctg	gccgccctcc	gcgagctaga	cgccgccgcc	3300
ccaggggacg	agcccgcccc	ccccgcggcc	ctgccctccc	cggccaagcg	ccccgggag	3360
acgccgtcgc	ctgccgaccc	cccgggaggc	gcgtccaagc	cccgcaagct	gctggtgtcc	3420
gagctggccg	aggatcccgc	atacgccatt	gcccacggcg	tegecetgaa	cacggactat	3480
tacttctccc	acctgttggg	ggeggegtge	gtgacattca	aggccctgtt	tgggaataac	3540
gccaagatca	ccgagagtct	gttaaaaagg	tttattcccg	aagtgtggca	cccccggac	3600
gacgtggccġ	cgcggctccg	gaccgcaggg	ttcggggcgg	tgggtgccgg	cgctacggcg	3660
gaggaaactc	gtcgaatgtt	gcatagagcc	tttgatactc	tagcatga		3708

<sup>&</sup>lt;210> 10

<400> 10

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg

<sup>&</sup>lt;211> 1235

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

155

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val 130

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr 165 170 175

150

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His
180 185 190

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn 195 200 205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu 210 215 220

Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe 225 230 235 240

Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr
245 250 255

Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr 260 265 270

Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro 275 280 285

Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile 290 295 300

Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro 305 310 315 320

Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly 325 330 335

Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile 340 345 350

Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp 355 360 365

Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala 370 375 380

Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp 385 390 395 400

Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser 405 410 415

Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu 420 425 430

Pro	Thr	Pro 435	Val	Val	Leu	Glu	Phe 440	Asp	Ser	Glu	Phe	Glu 445	Met	Leu	Leu	
Ala	Phe 450	Met	Thr	Leu	Val	Lys 455	Gln	Tyr	Gly	Pro	Glu 460	Phe	Val	Thr	Gly	
Tyr 465	Asn	Ile	Ile	Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480	
Asp	Ile	Tyr	Lys	Val 485	Pro	Leu	Asp	Gly	Tyr 490	Gly	Arg	Met	Asn	Gly 495	Arg	
Gly	Val	Phe	Arg 500	Val	Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg	
Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile	
Ile	Thr 530	Asp	Lys	Ile	Lys	Leu 535	Ser	Ser	Tyr	Lys	Leu 540	Asn	Ala	Val	Ala	
Glu 545	Ala	Val	Leu	Lys	Asp 550	Lys	Lys	Lys	Asp	Leu 555	Ser	Tyr	Arg	Asp	Ile 560	
Pro	Thr	Tyr	Tyr	Ala 565	Ala	Gly	Pro	Ala	Gln 570	Arg	Gly	Val	Ile	Gly 575	Glu	
Tyr	Cys	Ile	Gln 580	Asp	Ser	Leu	Leu	Val 585	Gly	Gln	Leu	Phe	Phe 590	Lys	Phe	
Leu	Pro	His 595	Leu	Glu	Leu	Ser	Ala 600	Val	Ala	Arg	Leu	Ala 605	Gly	Ile	Asn	
Ile	Thr 610	Arg	Thr	Ile	Tyr	Asp 615	Gly	Gln	Gln	Ile	Arg 620	Val	Phe	Thr	Cys	
Leu 625	Leu	Arg	Leu	Ala	Asp 630	Gln	Lys	Gly	Phe	Ile 635	Leu	Pro	Asp	Thr	Gln 640	
Gly	Arg	Phe	Arg	Gly 645	Ala	Gly	Gly	Glu	Ala 650	Pro	Lys	Arg	Pro	Ala 655	Ala	
Ala	Arg	Glu	Asp 660	Glu	Glu	Arg	Pro	Glu 665	Glu	Glu	Gly	Glu	Asp 670	Glu	Asn	
G1u	Arg	Glu 675	Glu	Gly	Gly	Gly	Glu 680	Arg	Glu	Pro	Glu	Gly 685	Ala	Arg	Glu	
Thr	Ala 690	Gly	Arg	His	Val	Gly 695	Tyr	Gln	Gly	Ala	Arg 700	Val	Leu	Asp	Pro	
Thr 705	Ser	Gly	Phe	His	Val 710	Asn	Pro	Val	Val,	Val 715	Phe	Asp	Phe	Ala	Ser 720	
Leu	Tyr	Pro	Ser	Ile 725	Ile	Gln	Ala	His	Asn 730	Leu	Сув	Phe	Ser	Thr 735	Leu	
Ser	Leu	Arg	Ala 740	Asp	Ala	Val	Ala	His 745	Leu	Glu	Ala	Gly	Lys 750	Asp	Tyr	·
Leu	Glu	Ile 755	Glu	Val	Gly	Gly	Arg 760	Arg	Leu	Phe	Phe	Val 765	Lys	Ala	His	

Val	Arg 770	Glu	Ser	Leu	Leu	Ser 775	Ile	Leu	Leu	Arg	Asp 780	Trp	Leu	Ala	Met
Arg 785	Lys	Gln	Ile	Arg	Ser 790	Arg	Ile	Pro	Gln	Ser 795	Ser	Pro	Glu	Glu	Ala 800
Val	Leu	Leu	Asp	Lys 805	Gln	Gln	Ala	Ala	Ile 810	Lys	Val	Val	Cys	Asn 815	Ser
Val	Tyr	Gly	Phe 820	Thr	Gly	Ala	Gln	His 825	Gly	Leu	Leu	Pro	Cys 830	Leu	His
Val	Ala	Ala 835	Thr	Val	Thr	Thr	Ile 840	Gly	Arg	Glu	Met	Leu 845	Leu	Ala	Thr
Arg	Glu 850	Tyr	Val	His	Ala	Arg 855	Trp	Ala	Ala	Phe	Glu 860	Gln	Leu	Leu	Ala
Asp 865	Phe	Pro	Glu	Ala	Ala 870	Asp	Met	Arg	Ala	Pro 875	Gly	Pro	Tyr	Ser	Met 880
Arg	Ile	Ile	Tyr	Gly 885	Asp	Thr	Asp	Ser	Ile 890	Phe	Val	Leu	Суѕ	Arg 895	Gly
Leu	Thr	Ala	Ala 900	Gly	Leu	Thr	Ala	Val 905	Gly	Asp	Lys	Met	Ala 910	Ser	His
Ile	Ser	Arg 915	Ala	Leu	Phe	Leu	Pro 920	Pro	Ile	Lys	Leu	G1u 925	Cys	Glu	Lys
Thr	Phe 930	Thr	Lys	Leu	Leu	Leu 935	Ile	Ala	Lys	Lys	Lys 940	Tyr	Ile	Gly	Val
Ile 945	Tyr	Gly	Gly	Lys	Met 950	Leu	Ile	Lys	Gly	Val 955		Leu	Val	Arg	Lys 960
Asn	Asn	Суз	Ala	Phe 965	Ile	Asn	Arg	Thr	Ser 970		Ala	Leu	Val	Asp 975	Leu
Leu	Phe	Tyr	Asp 980	Asp	Thr	Val	Ser	Gly 985	Ala	Ala	Ala	Ala	Leu 990	Ala '	Glu
Arg	Pro	Ala 995	Glu	Glu	Trp	Leu	Ala 1000		g Pr	o Le	u Pr		u G 05	ly L	eu Gln
Ala	Phe 1010		y Ala	a Val	l Leu	10:		sp A	la H	is A		rg 020	Ile	Thr .	Asp
Pro	Glu 1025	-	g Ası	o Il€	∋ Glr	10:		he V	al L	eu T		la 035	Glu	Leu	Ser
Arg	His 1040		o Ar	g Ala	а Туг	Th:		sn L	ys A	rg L		la 050	His	Leu	Thr
Val	Tyr 1055		r Ly:	s Lei	ı Met	10		rg A	rg A	la G		al 065	Pro	Ser	Ile
Lys	Asp 1070		g Ile	e Pro	о Туг	7 Va 10		le V	al A	la G		hr ' 080	Arg	Glu	Val
Glu	Glu	Th	r Va	l Ala	a Arc	, Le	u A	la A	la I	eu A	rg G	lu	Leu	Asp	Ala

	1085					1090					1095				
	Ala 1100	Pro	Gly	Asp	Glu	Pro 1105	Ala	Pro	Pro	Ala	Ala 1110	Leu	Pro	Ser	
	Ala 1115	Lys	Arg	Pro	Arg	Glu 1120	Thr	Pro	Ser	Pro	Ala 1125	Asp	Pro	Pro	
_	Gly 1130	Ala	Ser	Lys	Pro	Arg 1135	Lys	Leu	Leu	Val	Ser 1140	Glu	Leu	Ala	
	Asp 1145	Pro	Ala	Tyr	Ala	Ile 1150	Ala	His	Gly	Val	Ala 1155	Leu	Asn	Thr	
	Tyr 1160	Tyr	Phe	Ser	His	Leu 1165	Leu	Gly	Ala	Ala	Cys 1170	Val	Thr	Phe	
Lys	Ala 1175	Leu	Phe	Gly	Asn	Asn 1180	Ala	Lys	Ile	Thr	Glu 1185	Ser	Leu	Leu	
Lys	Arg 1190	Phe	Ile	Pro	Glu	Val 1195	Trp	His	Pro	Pro	Asp 1200	Asp	Val	Ala	
Ala	Arg 1205	Leu	Arg	Thr	Ala	Gly 1210	Phe	Gly	Ala	Val	Gly 1215	Ala	Gly	Ala	
Thr	Ala 1220	Glu	Glu	Thr	Arg	Arg 1225	Met	Leu	His	Arg	Ala 1230	Phe	Asp	Thr	
Leu	Ala 1235														
<212	.> 3'	729 NA	s siı	mple:	×										
<400						•									
atgt	tttt	ca a	ccca	tatc	t ga	gegge	ggc (	gtga	ccgg	cg g	tgcgg	tcgc	ggg†	ggccgg	
cgto	agcg	tt c	gcag	cccg	g ct	ccgcg	cag (	ggct	cggg	ca a	gegge	cgcc	acag	gaaacag	
tttt	tgca	ga to	cgtg	ccgc	g ag	gtgtc	atg	ttcg	acgg:	tc a	gacgg	ggtt	gate	caagcat	180
aaga	cggg	ac g	gctg	cctc	t ca	tgttc	tat (	cgag	agat	ta a	acatt	tgtt	gag	catgac	240
atgg	gtttg	gc c	gtgt	cctt	g gc	gcgag	acc	ctgg	tggg	tc g	cgtgg	tggg	acc	tattcgt	300
tttc	cacac	ct a	cgat	caga	c gg	acgcc	gtg	ctct	tctt	cg a	ctcgc	ccga	aaa	cgtgtcg	360
ccgc	gctai	tc g	tcag	catc	t gg	tgcct	tcg	ggga	acgt	gt t	gcgtt	tctt	cgg	ggccaca	420
gaac	cacgg	ct a	cagt	atct	g cg	tcaac	gtt	ttcg	ggca	gc g	cagct	actt	tta	ctgtgag	480
taca	agcga	ca c	cgat	aggc	t gc	gtgag	gtc .	attg	ccag	cg t	gggcg	aact	agt	gcccgaa	540
ccgc	ggac	gc c	atac	gccg	t gt	ctgtc	acg	ccgg	ccac	ca a	gacct	ccat	cta <sup>.</sup>	tgggtac	6.00
ggga	acgcga	ac c	cgtg	cccg	a tt	tgcag	tgt	gtgt	ctat	ca g	caact	ggac	cat	ggccaga	660
aaaa	tcgg	cg a	gtat	ctgc	t gg	agcag	ggt	tttc	ccgt	gt a	cgagg	tccg	tgt	ggatccg	720

ctgacgcgtt	tggtcatcga	tcggcggatc	accacgttcg	gctggtgctc	cgtgaatcgt	780
tacgactggc	ggcagcaggg	tcgcgcgtcg	acttgtgata	tcgaggtaga	ctgcgatgtc	840
tctgacctgg	tggctgtgcc	cgacgacagc	tcgtggccgc	gctatcgatg	cctgtccttc	900
gatatcgagt	gcatgagcgg	cgagggtggt	tttccctgcg	ccgagaagtc	cgatgacatt	960
gtcattcaga	tctcgtgcgt	gtgctacgag	acggggggaa	acaccgccgt	ggatcagggg	1020
atcccaaacg	ggaacgatgg	teggggetge	acttcggagg	gtgtgatctt	tgggcactcg	1080
ggtcttcatc	tctttacgat	cggcacctgc	gggcaggtgg	gcccagacgt	ggacgtctac	1140
gagttccctt	ccgaatacga	gctgctgctg	ggctttatgc	ttttctttca	acggtacgcg	1200
ccggcctttg	tgaccggtta	caacatcaac	tcttttgact	tgaagtacat	cctcacgcgt	1260
ctcgagtacc	tgtataaggt	ggactcgcag	cgcttctgca	agttgcctac	ggcgcagggc	1320
ggccgtttct	ttttacacag	ccccgccgtg	ggttttaagc	ggcagtacgc	cgccgctttt	1380
ccctcggctt	ctcacaacaa	teeggeeage	acggccgcca	ccaaggtgta	tattgcgggt	1440
tcggtggtta	tcgacatgta	ccctgtatgc	atggccaaga	ctaactcgcc	caactataag	1500
ctcaacacta	tggccgagct	ttacctgcgg	caacgcaagg	atgacctgtc	ttacaaggac	1560
atcccgcgtt	gtttcgtggc	taatgccgag	ggccgcgccc	aggtaggccg	ttactgtctg	1620
caggacgccg	tattggtgcg	cgatctgttc	aacaccatta	attttcacta	cgaggccggg	1680
gccatcgcgc	ggctggctaa	aattccgttg	cggcgtgtca	tctttgacgg	acagcagatc	1740
cgtatctaca	cctcgctgct	ggacgagtgc	gcctgccgcg	attttatcct	gcccaaccac	1800
tacagcaaag	gtacgacggt	gcccgaaacg	aatagcgttg	ctgtgtcacc	taacgctgct	1860
atcatctcta	ccgccgctgt	gcccggcgac	gcgggttctg	tggcggctat	gtttcagatg	1920
tegeegeeet	tgcaatctgc	gccgtccagt	caggacggcg	tttcacccgg	ctccggcagt	1980
aacagtagta	gcagcgtcgg	cgttttcagc	gtcggctccg	gcagtagtgg	cggcgtcggc	2040
gtttccaacg	acaatcacgg	cgccggcggt	actgcggcgg	tttcgtacca	gggcgccacg	2100
gtgtttgagc	ccgaggtggg	ttactacaac	gaccccgtgg	ccgtgttcga	ctttgccagc	2160
ctctaccctt	ccatcatcat	ggcccacaac	ctctgctact	ccaccctgct	ggtgccgggt	2220
ggcgagtacc	ctgtggaccc	cgccgacgta	tacagcgtca	cgctagagaa	cggcgtgacc	2280
caccgctttg	tgcgtgcttc	ggtgcgcgtc	teggtgetet	cggaactgct	caacaagtgg	2340
gtttcgcagc	ggcgtgccgt	gcgcgaatgc	atgcgcgagt	gtcaagaccc	tgtgcgccgt	2400
atgctgctcg	acaaggaaca	gatggcgctc	aaagtaacgt	gcaacgcttt	ctacggtttt	2460
accggcgcgc	tgaacggtat	gatgccgtgt	ctgcccatcg	ccgccagcat	cacgcgcatc	2520
ggtcgcgaca	tgctagagcg	cacggcgcgg	ttcatcaaag	acaactttc	agagccgtgt	2580

tttttgcaca	atttttttaa	tcaggaagac	tatgtagtgg	gaacgcggga	gggggattcg	2640
gaggagagca	gcgcgttacc	ggaggggctc	gaaacatcgt	cagggggctc	gaacgaacgg	2700
cgggtggagg	cgcgggtcat	ctacggggac	acggacagcg	tgtttgtccg	ctttcgtggc	2760
ctgacgccgc	aggctctggt	ggcgcgtggg	cccagcctgg	cgcactacgt	gacggcctgt	2820
ctttttgtgg	agcccgtcaa	gctggagttt	gaaaaggtct	tegtetetet	tatgatgatc	2880
tgcaagaaac	gttacatcgg	caaagtggag	ggcgcctcgg	gtctgagcat	gaagggcgtg	2940
gatctggtgc	gcaagacggc	ctgcgagttc	gtcaagggcg	tcacgcgtga	cgtcctctcg	3000
ctgctctttg	aggatcgcga	ggtctcggaa	gcagccgtgc	gcctgtcgcg	cctctcactc	3060
gatgaagtca	agaagtacgg	cgtgccacgc	ggtttctggc	gtatcttacg	ccgcttggtg	3120
caggcccgcg	acgatctgta	cctgcaccgt	gtgcgtgtcg	aggacctggt	gctttcgtcg	3180
gtgctctcta	aggacatctc	gctgtaccgt	caatctaacc	tgccgcacat	tgccgtcatt	3240
aagcgattgg	cggcccgttc	tgaggagcta	ccctcggtcg	gggatcgggt	cttttacgtt	3300
ctgacggcgc	ccggtgtccg	gacggcgccg	cagggttcct	ccgacaacgg	tgattctgta	3360
accgccggcg	tggtttcccg	gtcggacgcg	attgatggca	cggacgacga	cgctgacggc	3420
ggcggggtag	aggagagcaa	caggagagga	ggagagccgg	caaagaagag	ggcgcggaaa	3480
ccaccgtcgg	ccgtgtgcaa	ctacgaggta	gccgaagatc	cgagctacgt	gcgcgagcac	3540
ggcgtgccca	ttcacgccga	caagtacttt	gagcaggttc	tcaaggctgt	aactaacgtg	3600
ctgtcgcccg	tettteeegg	cggcgaaacc	gcgcgcaagg	acaagttttt	gcacatggtg	3660
ctgccgcggc	gcttgcactt	ggagccggct	tttctgccgt	acagtgtcaa	ggcgcacgaa	3720
tgctgttga						3729

<sup>&</sup>lt;210> 12

Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Gly Ala Val 1 5 10 15

Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser 20 25 30

Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly 35 40 45

Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg 50 55 60

Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp 65 70 75 80

<sup>&</sup>lt;211> 1242

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> herpes simplex

<sup>&</sup>lt;400> 12

Met Val Ti	p Pro Cy: 85	s Pro Trp	Arg	Glu	Thr 90	Leu	Val	Gly	Arg	Val 95	Val
Gly Pro II	e Arg Pho	e His Th	Tyr	Asp 105	Gln	Thr	Asp	Ala	Val 110	Leu	Phe
Phe Asp Se		ı Asn Val	Ser 120	Pro	Arg	Tyr	Arg	Gln 125	His	Leu	Val
Pro Ser G	y Asn Val	L Leu Arg 135		Phe	Gly	Ala	Thr 140	Glu	His	Gly	Tyr
Ser Ile Cy 145	s Val Ası	n Val Phe 150	e Gly	Gln	Arg	Ser 155	Tyr	Phe	Tyr	Cys	Glu 160
Tyr Ser As	p Thr Ası 16!		ı Arg	Glu	Val 170	Ile	Ala	Ser	Val	Gly 175	Glu
Leu Val Pi	o Glu Pro 180	Arg Thi	Pro	Tyr 185	Ala	Val	Ser	Val	Thr 190	Pro	Ala
Thr Lys Th		∍ Tyr Gly	7 Туг 200	Gly	Thr	Arg	Pro	Val 205	Pro	Asp	Leu
Gln Cys Va 210	l Ser Ile	e Ser Ası 215	_	Thr	Met	Ala	Arg 220	Lys	Ile	Gly	Glu
Tyr Leu Le 225	u Glu Glı	n Gly Phe 230	∍ Pro	Val	Tyr	Glu 235	Val	Arg	Val	Asp	Pro 240
Leu Thr Ai	g Leu Val 24!	_	Arg	Arg	Ile 250	Thr	Thr	Phe	Gly	Trp 255	Cys
Ser Val As	n Arg Ty 260	r Asp Tr	Arg	Gln 265	Gln	Gly	Arg	Ala	Ser 270	Thr	Cys
Asp Ile G	-	o Cys Ası	280	Ser	Asp	Leu	Val	Ala 285	Val	Pro	Asp
Asp Ser Se 290	r Trp Pro	Arg Ty:	_	Сув	Leu	Ser	Phe 300	Asp	Ile	Glu	Суз
Met Ser G	y Glu Gly	Gly Phe	e Pro	Cys	Ala	Glu 315	Lys	Ser	Asp	Asp	Ile 320
Val Ile G	n Ile Ser 325		Cys	Tyr	Glu 330	Thr	Gly	Gly	Asn	Thr 335	Ala
Val Asp G	n Gly Ile 340	e Pro Ası	ı Gly	Asn 345	Asp	Gly	Arg	Gly	Суs 350	Thr	Ser
Glu Gly Va		e Gly His	360	Gly	Leu	His	Leu	Phe 365	Thr	Ile	Gly
Thr Cys G	y Gln Vai	Gly Pro	_	Val	Asp	Val	Tyr 380	Glu	Phe	Pro	Ser
Glu Tyr G 385	u Leu Lei	ı Leu Gly 390	7 Phe	Met	Leu	Phe 395	Phe	Gln	Arg	Tyr	Ala 400
Pro Ala Pi	e Val Th	Gly Ty	: Asn	Ile	Asn	Ser	Phe	Asp	Leu	Lys	Tyr

405 410 415 Ile Leu Thr Arg Leu Glu Tyr Leu Tyr Lys Val Asp Ser Gln Arg Phe 425 Cys Lys Leu Pro Thr Ala Gln Gly Gly Arg Phe Phe Leu His Ser Pro Ala Val Gly Phe Lys Arg Gln Tyr Ala Ala Ala Phe Pro Ser Ala Ser His Asn Asn Pro Ala Ser Thr Ala Ala Thr Lys Val Tyr Ile Ala Gly 470 475 Ser Val Val Ile Asp Met Tyr Pro Val Cys Met Ala Lys Thr Asn Ser 485 Pro Asn Tyr Lys Leu Asn Thr Met Ala Glu Leu Tyr Leu Arg Gln Arg 505 Lys Asp Asp Leu Ser Tyr Lys Asp Ile Pro Arg Cys Phe Val Ala Asn 520 Ala Glu Gly Arg Ala Gln Val Gly Arg Tyr Cys Leu Gln Asp Ala Val Leu Val Arg Asp Leu Phe Asn Thr Ile Asn Phe His Tyr Glu Ala Gly Ala Ile Ala Arg Leu Ala Lys Ile Pro Leu Arg Arg Val Ile Phe Asp 570 Gly Gln Gln Ile Arg Ile Tyr Thr Ser Leu Leu Asp Glu Cys Ala Cys Arg Asp Phe Ile Leu Pro Asn His Tyr Ser Lys Gly Thr Thr Val Pro 600 Glu Thr Asn Ser Val Ala Val Ser Pro Asn Ala Ala Ile Ile Ser Thr 610 615 620 Ala Ala Val Pro Gly Asp Ala Gly Ser Val Ala Ala Met Phe Gln Met 630 635 Ser Pro Pro Leu Gln Ser Ala Pro Ser Ser Gln Asp Gly Val Ser Pro 645 650 Gly Ser Gly Ser Asn Ser Ser Ser Ser Val Gly Val Phe Ser Val Gly 665 Ser Gly Ser Ser Gly Gly Val Gly Val Ser Asn Asp Asn His Gly Ala Gly Gly Thr Ala Ala Val Ser Tyr Gln Gly Ala Thr Val Phe Glu Pro Glu Val Gly Tyr Tyr Asn Asp Pro Val Ala Val Phe Asp Phe Ala Ser 715 Leu Tyr Pro Ser Ile Ile Met Ala His Asn Leu Cys Tyr Ser Thr Leu

730

35

Leu	Val	Pro	Gly 740	Gly	Glu	Tyr	Pro	Va1 745	Asp	Pro	Ala	Asp	Val 750	Tyr	Ser
Val	Thr	Leu 755	Glu	Asn	Gly	Val	Thr 760	His	Arg	Phe	Val	Arg 765	Ala	Ser	Val
Arg	Val 770	Ser	Val	Leu	Ser	Glu 775	Leu	Leu	Asn	Lys	Trp 780	Val	Ser	Gln	Arg
Arg 785	Ala	Val	Arg	Glu	Cys 790	Met	Arg	Glu	Cys	Gln 795	Asp	Pro	Val	Arg	Arg 800
Met	Leu	Leu	Asp	Lys 805	Glu	Gln	Met	Ala	Leu 810	Lys	Val	Thr	Cys	Asn 815	Ala
Phe	Tyr	Gly	Phe 820	Thr	Gly	Ala	Leu	Asn 825	Gly	Met	Met	Pro	Cys	Leu	Pro
Ile	Ala	Ala 835	Ser	Ile	Thr	Arg	Ile 840	Gly	Arg	Asp	Met	Leu 845	Glu	Arg	Thr
Ala	Arg 850	Phe	Ile	Lys	Asp	Asn 855	Phe	Ser	Glu	Pro	860 850	Phe	Leu	His	Asn
Phe 865	Phe	Asn	Gln	Glu	Asp 870	Tyr	Val	Val	Gly	Thr 875	Arg	Glu	G1y	Asp	Ser 880
Glu	Glu	Ser	Ser	Ala 885	Leu	Pro	Glu	Gly	Leu 890	Glu	Thr	Ser	Ser	Gly 895	Gly
Ser	Asn	Glu	Arg 900	Arg	Val	Glu	Ala	Arg 905	Val	Ile	Tyr	Gly	Asp 910	Thr	Asp
Ser	Val	Phe 915	Val	Arg	Phe	Arg	Gly 920	Leu	Thr	Pro	Gln	Ala 925	Leu	Val	Ala
Arg	Gly 930	Pro	Ser	Leu	Ala	His 935	Tyr	Val	Thr	Ala	Cys 940	Leu	Phe	Val	Glu
Pro 945	Val	Lys	Leu	Glu	Phe 950	Glu	Lys	Val	Phe	Val 955	Ser	Leu	Met	Met	Ile 960
Cys	Lys	Lys	Arg	Tyr 965	Ile	Gly	Lys	Val	Glu 970	Gly	Ala	Ser	Gly	Leu 975	Ser
Met	Lys	Gly	Val 980	Asp	Leu	Val	Arg	Lys 985	Thr	Ala	Cys	Glu	Phe 990	Val	Lys
Gly	Val	Thr 995	Arg	Asp	Va1	Leu	Ser 1000		ı Leı	ı Phe	e Glu	ı Ası 100		rg G	lu Val
Ser	Glu 1010		a Ala	a Val	Arg	j Let 101		er Ai	g Le	eu Se		eu 1 020	Asp (	Glu '	Val
Lys	Lys 1025		Gl3	y Val	L Pro	103	-	Ly Ph	ıe Tı	cp Ar	_	le 1 035	Leu A	Arg .	Arg
Leu	Val 1040		n Ala	a Arç	g Asp	Asp 104		eu T∑	yr Le	eu Hi		rg 7 050	Val 1	Arg '	Val
Glu	Asp 1055		ı Val	Leu	ı Sei	Ser 106		al Le	eu S∈	er Ly		sp :	Ile S	Ser :	Leu

Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu 1075 1070 Ala Ala Arg Ser Glu Glu Leu Pro Ser Val Gly Asp Arg Val Phe 1090 Tyr Val Leu Thr Ala Pro Gly Val Arg Thr Ala Pro Gln Gly Ser 1105 Ser Asp Asn Gly Asp Ser Val Thr Ala Gly Val Val Ser Arg Ser 1120 1125 1115 Asp Ala Ile Asp Gly Thr Asp Asp Asp Ala Asp Gly Gly Val 1135 Glu Glu Ser Asn Arg Arg Gly Gly Glu Pro Ala Lys Lys Arg Ala 1150 1155 Arg Lys Pro Pro Ser Ala Val Cys Asn Tyr Glu Val Ala Glu Asp Pro Ser Tyr Val Arg Glu His Gly Val Pro Ile His Ala Asp Lys Tyr Phe Glu Gln Val Leu Lys Ala Val Thr Asn Val Leu Ser Pro 1195 Val Phe Pro Gly Gly Glu Thr Ala Arg Lys Asp Lys Phe Leu His 1210 Met Val Leu Pro Arg Arg Leu His Leu Glu Pro Ala Phe Leu Pro 1225 Tyr Ser Val Lys Ala His Glu Cys Cys 1240 1235 <210> 13 <211> 1242 <212> PRT <213> herpes simplex <400> 13 Met Phe Phe Asn Pro Tyr Leu Ser Gly Gly Val Thr Gly Gly Ala Val 1 5 Ala Gly Gly Arg Arg Gln Arg Ser Gln Pro Gly Ser Ala Gln Gly Ser 25 Gly Lys Arg Pro Pro Gln Lys Gln Phe Leu Gln Ile Val Pro Arg Gly 40 Val Met Phe Asp Gly Gln Thr Gly Leu Ile Lys His Lys Thr Gly Arg Leu Pro Leu Met Phe Tyr Arg Glu Ile Lys His Leu Leu Ser His Asp Met Val Trp Pro Cys Pro Trp Arg Glu Thr Leu Val Gly Arg Val Val 90

Gly Pro Il	e Arg Phe 100	His Thr	Tyr	Asp 105	Gln	Thr	Asp	Ala	Val 110	Leu	Phe
Phe Asp Se 11		. Asn Val	Ser 120	Pro	Arg	Tyr	Arg	Gln 125	His	Leu	Val
Pro Ser Gl	y Asn Val	Leu Arg 135		Phe	Gly	Ala	Thr 140	Glu	His	Gly	Tyr
Ser Ile Cy 145	s Val Asn	Val Phe	e Gly	Gln	Arg	Ser 155	Tyr	Phe	Tyr	Cys	Glu 160
Tyr Ser As	p Thr Asp 165	<del>-</del>	Arg	Glu	Val 170	Ile	Ala	Ser	Val	Gly 175	Glu
Leu Val Pr	o Glu Pro 180	Arg Thr	Pro	Tyr 185	Ala	Val	Ser	Val	Thr 190	Pro	Ala
Thr Lys Th 19		Tyr Gly	Tyr 200	Gly	Thr	Arg	Pro	Val 205	Pro	Asp	Leu
Gln Cys Va 210	l Ser Ile	Ser Asr 215		Thr	Met	Ala	Arg 220	Lys	Ile	Gly	Glu
Tyr Leu Le 225	u Glu Gln	Gly Phe	Pro	Val	Tyr	Glu 235	Val	Arg	Val	Asp	Pro 240
Leu Thr Ar	g Leu Val 245	-	Arg	Arg	Ile 250	Thr	Thr	Phe	Gly	Trp 255	Cys
Ser Val As	n Arg Tyr 260	Asp Trp	Arg	Gln 265	Gln	Gly	Arg	Ala	Ser 270	Thr	Cys
Asp Ile Gl	5		280					285			
Asp Ser Se 290		295					300				
Met Ser Gl	_	310		_		315					320
Val Ile Gl	325	_	_	_	330		_	-		335	
Val Asp Gl	340			345					350	_	_
Glu Gly Va 35	5		360					365			
Thr Cys Gl		375	-		_		380				
Glu Tyr Gl 385		390				395					400
Pro Ala Ph	405				410					415	
Ile Leu Th	r Arg Leu 420	Glu Tyr	Leu	Tyr 425	Lys	Val	Asp	Ser	Gln 430	Arg	Phe

Cys	Lys	Leu 435	Pro	Thr	Ala	Gln	Gly 440	Gly	Arg	Phe	Phe	Leu 445	His	Ser	Pro
Ala	Val 450	Gly	Phe	Lys	Arg	Gln 455	Tyr	Ala	Ala	Ala	Phe 460	Pro	Ser	Ala	Ser
His 465	Asn	Asn	Pro	Ala	Ser 470	Thr	Ala	Ala	Thr	Lys 475	Val	Tyr	Ile	Ala	Gly 480
Ser	Val	Val	Ile	Asp 485	Met	Tyr	Pro	Val	Cys 490	Met	Ala	Lys	Thr	Asn 495	Ser
Pro	Asn	Tyr	Lуs 500	Leu	Asn	Thr	Met	Ala 505	Glu	Leu	Tyr	Leu	Arg 510	Gln	Arg
Lys	Asp	Asp 515	Leu	Ser	Tyr	Lys	Asp 520	Ile	Pro	Arg	Cys	Phe 525	Val	Ala	Asn
Ala	Glu 530	Gly	Arg	Ala	Gln	Val 535	Gly	Arg	Tyr	Cys	Leu 540	Gln	Asp	Ala	Val
Leu 545	Val	Arg	Asp	Leu	Phe 550	Asn	Thr	Ile	Asn	Phe 555	His	Tyr	Glu	Ala	Gly 560
Ala	Ile	Ala	Arg	Leu 565	Ala	Lys	Ile	Pro	Leu 570	Arg	Arg	Val	Ile	Phe 575	Asp
Gly	Gln	Gln	Ile 580	Arg	Ile	Tyr	Thr	Ser 585	Leu	Leu	Asp	Glu	Cys 590	Ala	Cys
Arg	Asp	Phe 595	Ile	Leu	Pro	Asn	His 600	Tyr	Ser	Lys	Gly	Thr 605	Thr	Val	Pro
Glu	Thr 610	Asn	Ser	Val	Ala	Val 615	Ser	Pro	Asn	Alá	Ala 620	Ile	Ile	Ser	Thr
Ala 625	Ala	Val	Pro	Gly	Asp 630	Ala	Gly	Ser	Val	Ala 635	Ala	Met	Phe	Gln	Met 640
Ser	Pro	Pro	Leu	Gln 645	Ser	Ala	Pro	Ser	Ser 650	Gln	Asp	Gly	Val	Ser 655	Pro
Gly	Ser	Gly	Ser 660	Asn	Ser	Ser	Ser	Ser 665	Val	Gly	Val	Phe	Ser 670	Val	Gly
Ser	Gly	Ser 675	Ser	Gly	Gly	Val	Gly 680	Val	Ser	Asn	Asp	Asn 685	His	Gly	Ala
Gly	Gly 690	Thr	Ala	Ala	Val	Ser 695	Tyr	Gln	Gly	Ala	Thr 700	Val	Phe	Glu	Pro
Glu 705	Val	Gly	Tyr	Tyr	Asn 710	Asp	Pro	Val	Ala	Val 715	Phe	Asp	Phe	Ala	Ser 720
Leu	Tyr	Pro	Ser	Ile 725	Ile	Met	Ala	His	Asn 730	Leu	Cys	Tyr	Ser	Thr 735	Leu
Leu	Val	Pro	Gly 740	Gly	Glu	Tyr	Pro	Val 745	Asp	Pro	Ala	Asp	Val 750	Tyr	Ser
Val	Thr	Leu	Glu	Asn	Gly	Val	Thr	His	Arg	Phe	Val	Arg	Ala	Ser	Val

WO 02/06513	PCT/US01/16525

755 760 765 Arg Val Ser Val Leu Ser Glu Leu Leu Asn Lys Trp Val Ser Gln Arg 775 Arg Ala Val Arg Glu Cys Met Arg Glu Cys Gln Asp Pro Val Arg Arg 795 790 Met Leu Leu Asp Lys Glu Gln Met Ala Leu Lys Val Thr Cys Asn Ala 805 81.0 Phe Tyr Gly Phe Thr Gly Val Val Asn Gly Met Met Pro Cys Leu Pro 825 Ile Ala Ala Ser Ile Thr Arg Ile Gly Arg Asp Met Leu Glu Arg Thr Ala Arg Phe Ile Lys Asp Asn Phe Ser Glu Pro Cys Phe Leu His Asn 855 Phe Phe Asn Gln Glu Asp Tyr Val Val Gly Thr Arg Glu Gly Asp Ser 870 Glu Glu Ser Ser Ala Leu Pro Glu Gly Leu Glu Thr Ser Ser Gly Gly 885 890 Ser Asn Glu Arg Arg Val Glu Ala Arg Val Ile Tyr Gly Asp Thr Asp 900 905 Ser Val Phe Val Arg Phe Arg Gly Leu Thr Pro Gln Ala Leu Val Ala 920 Arg Gly Pro Ser Leu Ala His Tyr Val Thr Ala Cys Leu Phe Val Glu 930 Pro Val Lys Leu Glu Phe Glu Lys Val Phe Val Ser Leu Met Met Ile 955 Cys Lys Lys Arg Tyr Ile Gly Lys Val Glu Gly Ala Ser Gly Leu Ser Met Lys Gly Val Asp Leu Val Arg Lys Thr Ala Cys Glu Phe Val Lys Gly Val Thr Arg Asp Val Leu Ser Leu Leu Phe Glu Asp Arg Glu Val Ser Glu Ala Ala Val Arg Leu Ser Arg Leu Ser Leu Asp Glu Val 1015 1020 1010 Lys Lys Tyr Gly Val Pro Arg Gly Phe Trp Arg Ile Leu Arg Arg 1035 1025 1030 Leu Val Gln Ala Arg Asp Asp Leu Tyr Leu His Arg Val Arg Val 1045 1050 Glu Asp Leu Val Leu Ser Ser Val Leu Ser Lys Asp Ile Ser Leu 1060 1065 Tyr Arg Gln Ser Asn Leu Pro His Ile Ala Val Ile Lys Arg Leu 1070 1075 1080

Ala Ala Arg Ser Glu Glu Leu Pro Ser Val Gly Asp Arg Val Phe 1090 Tyr Val Leu Thr Ala Pro Gly Val Arg Thr Ala Pro Gln Gly Ser 1105 Ser Asp Asn Gly Asp Ser Val Thr Ala Gly Val Val Ser Arg Ser 1120 Asp Ala Ile Asp Gly Thr Asp Asp Asp Ala Asp Gly Gly Val 1135 1130 Glu Glu Ser Asn Arg Arg Gly Gly Glu Pro Ala Lys Lys Arg Ala 1145 1150 1155 Arg Lys Pro Pro Ser Ala Val Cys Asn Tyr Glu Val Ala Glu Asp 1165 Pro Ser Tyr Val Arg Glu His Gly Val Pro Ile His Ala Asp Lys 1180 1175 Tyr Phe Glu Gln Val Leu Lys Ala Val Thr Asn Val Leu Ser Pro 1195 Val Phe Pro Gly Gly Glu Thr Ala Arg Lys Asp Lys Phe Leu His 1210 1205 Met Val Leu Pro Arg Arg Leu His Leu Glu Pro Ala Phe Leu Pro 1225 1230 Tyr Ser Val Lys Ala His Glu Cys Cys 1235 1240 <210> 14 <211> 1238 <212> PRT <213> herpes simplex <400> 14 Met Phe Cys Ala Ala Gly Gly Pro Thr Ser Pro Gly Gly Lys Ser Ala Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala Thr Gln Thr Ala Pro Pro Pro Cys Arg Gln Asn Phe Tyr Asn Pro 40 His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro 70 Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His 90 Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu 100 110 105 Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu

120 115 125 Arg Leu Trp Gly Gly Ala Asp His Ala Pro Lys Gly Phe Asp Pro Thr 135 Val Thr Val Phe His Val Tyr Asp Ile Leu Glu His Val Glu His Ala 155 Tyr Ser Met Arg Ala Ala Gln Leu His Glu Arg Phe Met Asp Ala Ile 170 Thr Pro Ala Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly 185 His Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn Lys Ala Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu Cys Glu Arg Leu Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg 250 Ala Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Thr Leu Tyr Tyr Arg Val Phe Val Arg Ser Gly Arg Ala Leu Ala Tyr Leu Cys Asp Asn Phe Cys 280 Pro Ala Ile Arg Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe 290 Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys 310 315 Pro Gly Arg Gly Asn Ala Pro Ala Gln Pro Arg Pro Pro Thr Ala Phe 325 330 Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala 340 345 Val Glu Gly Ala Met Cys Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe 360 Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala Glu Arg Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr 390 395 Asp Leu Ser Thr Thr Ala Leu Glu His Ile Leu Leu Phe Ser Leu Gly 410 Ser Cys Asp Leu Pro Glu Ser His Leu Ser Asp Leu Ala Ser Arg Gly 425 Leu Pro Ala Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu 435 440

Leu Ala 450	Phe	Met	Thr	Phe	Val 455	Lys	Gln	Tyr	Gly	Pro 460	Glu	Phe	Val	Thr
Gly Tyr 465	Asn	Ile	Ile	Asn 470	Phe	Asp	Trp	Pro	Phe 475	Val	Leu	Thr	Lys	Leu 480
Thr Glu	Ile	Tyr	Lys 485	Val	Pro	Leu	Asp	Gly 490	Tyr	Gly	Arg	Met	Asn 495	Gly
Arg Gly	Val	Phe 500	Arg	Val	Trp	Asp	Ile 505	Gly	Gln	Ser	His	Phe 510	Gln	Lys
Arg Ser	Lys 515	Ile	Lys	Val	Asn	Gly 520	Met	Val	Asn	Ile	Asp 525	Met	Tyr	Gly
Ile Ile 530	Thr	Asp	Lys	Val	Lys 535	Leu	Ser	Ser	Tyr	Lys 540	Leu	Asn	Ala	Val
Ala Glu 545	Ala	Val	Leu	Lys 550	Asp	Lys	Lys	Lys	Asp 555	Leu	Ser	Tyr	Arg	Asp 560
Ile Pro	Ala	Tyr	Туr 565	Ala	Ser	Gly	Pro	Ala 570	Gln	Arg	Gly	Val	Ile 575	Gly
Glu Tyr	Cys	Val 580	Gln	Asp	Ser	Leu	Leu 585	Val	Gly	Gln	Leu	Phe 590	Phe	Lys
Phe Leu	Pro 595	His	Leu	Glu	Leu	Ser 600	Ala	Val	Ala	Arg	Leu 605	Ala	Gly	Ile
Asn Ile 610	Thr	Arg	Thr	Ile	Tyr 615	Asp	Gly	Gln	Gln	Ile 620	Arg	Val	Phe	Thr
Cys Leu 625	Leu	Arg	Leu	Ala 630	Gly	Gln	Lys	Gly	Phe 635	Ile	Leu	Pro	Asp	Thr 640
Gln Gly	Arg	Phe	Arg 645	Gly	Leu	Asp	Lys	Glu 650	Ala	Pro	Lys	Arg	Pro 655	Ala
Val Pro	Arg	Gly 660	Glu	Gly	Glu	Arg	Pro 665	Gly	Asp	Gly	Asn	Gly 670	Asp	Glu
Asp Lys	Asp 675	Asp	Asp	Glu	Asp	Glu 680	Asp	Gly	Asp	Glu	Arg 685	Glu	Glu	Val
Ala Arg 690	Glu	Thr	Gly	Gly	Arg 695	His	Val	Gly	Tyr	Gln 700	Gly	Ala	Arg	Val
Leu Asp 705	Pro	Thr	Ser	Gly 710	Phe	His	Val	Asp	Pro 715	Val	Val	Val	Phe	Asp 720
Phe Ala	Ser	Leu	Туг 725	Pro	Ser	Ile	Ile	Gln 730	Ala	His	Asn	Leu	Cys 735	Phe
Ser Thr	Leu	Ser 740	Leu	Arg	Pro	Glu	Ala 745	Val	Ala	His	Leu	Glu 750	Ala	Asp
Arg Asp	Tyr 755	Leu	Glu	Ile	Glu	Val 760	Gly	Gly	Arg	Arg	Leu 765	Phe	Phe	Val
Lys Ala 770	His	Val	Arg	Glu	Ser 775	Leu	Leu	Ser	Ile	Leu 780	Leu	Arg	Asp	Trp

Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Thr Pro 795 Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val 810 Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro 825 Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu 840 Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe Asp Gln 855 Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu 890 Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met 905 Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu 920 Cys Glu Lys Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu 955 950 Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu 970 Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala 985 Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg 1015 Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala 1030 1025 Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala 1045 1050 1040 His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val 1065 1055 1060 Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr 1070 1075 1080 Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu 1090 1095 Leu Asp Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala

1100 1105 1110

Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala 1115 1120 1125

- Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Val Ser 1130 1135 1140
- Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly Val Pro 1145 1150 1155
- Leu Asn Thr Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys 1160 1165 1170
- Val Thr Phe Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu 1175 1180 1185
- Ser Leu Leu Lys Arg Phe Ile Pro Glu Thr Trp His Pro Pro Asp 1190 1195 1200
- Asp Val Ala Ala Arg Leu Arg Ala Ala Gly Phe Gly Pro Ala Gly 1205 1210 1215
- Ala Gly Ala Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala 1220 1225 1230

Phe Asp Thr Leu Ala 1235

<210> 15

<211> 1240

<212> PRT

<213> herpes simplex

<400> 15

- Met Phe Cys Ala Ala Gly Gly Pro Ala Ser Pro Gly Gly Lys Ser Ala 1 5 10 15
- Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro His Asn Pro Arg Gly Ala 20 25 30
- Thr Gln Thr Ala Pro Pro Pro Cys Arg Gln Asn Phe Tyr Asn Pro 35 40 45
- His Leu Ala Gln Thr Gly Thr Gln Pro Lys Ala Pro Gly Pro Ala Gln 50 55 60
- Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro 65 70 75 80
- Arg Ser Leu Asp Glu Asp Ala Pro Ala Glu Gln Arg Thr Gly Val His
  85 90 95
- Asp Gly Arg Leu Arg Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu 100 105 110
- Arg Asp Val Leu Arg Val Gly Pro Glu Gly Phe Trp Pro Arg Arg Leu 115 120 125
- Arg Leu Trp Gly Gly Ala Asp His Ala Pro Glu Gly Phe Asp Pro Thr 130 135 140

Val 145	Thr	Val	Phe	His	Val 150	Tyr	Asp	Ile	Leu	Glu 155	His	Val	Glu	His	Ala 160
Tyr	Ser	Met	Arg	Ala 165	Ala	Gln	Leu	His	Glu 170	Arg	Phe	Met	Asp	Ala 175	Ile
Thr	Pro	Ala	Gly 180	Thr	Val	Ile	Thr	Leu 185	Leu	Gly	Leu	Thr	Pro 190	Glu	Gly
His	Arg	Val 195	Ala	Val	His	Val	Tyr 200	Gly	Thr	Arg	Gln	Tyr 205	Phe	Tyr	Met
Asn	Lys 210	Ala	Glu	Val	Asp	Arg 215	His	Leu	Gln	Cys	Arg 220	Ala	Pro	Arg	Asp
Leu 225	Cys	Glu	Arg	Leu	Ala 230	Ala	Ala	Leu	Arg	Glu 235	Ser	Pro	Gly	Ala	Ser 240
Phe	Arg	Gly	Ile	Ser 245	Ala	Asp	His	Phe	Glu 250	Ala	Glu	Val	Val	Glu 255	Arg
Ala	Asp	Val	Туr 260	Tyr	Tyr	Glu	Thr	Arg 265	Pro	Thr	Leu	Tyr	Tyr 270	Arg	Val
Phe	Val	Arg 275	Ser	Gly	Arg	Ala	Leu 280	Ala	Tyr	Leu	Cys	Asp 285	Asn	Phe	Cys
Pro	Ala 290	Ile	Arg	Lys	Tyr	Glu 295	Gly	Gly	Val	Asp	Ala 300	Thr	Thr	Arg	Phe
Ile 305	Leu	Asp	Asn	Pro	Gly 310	Phe	Val	Thr	Phe	Gly 315	Trp	Tyr	Arg	Leu	Lys 320
Pro	Gly	Arg	Gly	Asn 325	Ala	Pro	Ala	Gln	Pro 330	Arg	Pro	Pro	Thr	Ala 335	Phe
Gly	Thr	Ser	Ser 340	Asp	Val	Glu	Phe	Asn 345	Cys	Thr	Ala	Asp	Asn 350	Leu	Ala
Val	Glu	Gly 355	Ala	Met	Cys	Asp	Leu 360	Pro	Ala	Tyr	Lys	Leu 365	Met	Cys	Phe
Asp	Ile 370	Glu	Cys	Lys	Ala	Gly 375	Gly	Glu	Asp	Glu	Leu 380	Ala	Phe	Pro	Val
Ala 385	Glu	Arg	Pro	Glu	Asp 390	Leu	Val	Ile	Gln	Ile 395	Ser	Cys	Leu	Leu	Tyr 400
Asp	Leu	Ser	Thr	Thr 405	Ala	Leu	Glu	His	Ile 410	Leu	Leu	Phe	Ser	Leu 415	Gly
Ser	Cys	Asp	Leu 420	Pro	Glu	Ser	His	Leu 425	Ser	Asp	Leu	Ala	Ser 430	Arg	Gly
Leu	Pro	Ala 435	Pro	Val	Val	Leu	Glu 440	Phe	Asp	Ser	Glu	Phe	Glu	Met	Leu
Leu	Ala 450	Phe	Met	Thr	Phe	Val 455	Lys	Gln	Tyr	Gly	Pro 460	Glu	Phe	Val	Thr
Gly	Tyr	Asn	Ile	Ile	Asn	Phe	Asp	Trp	Pro	Phe	Val	Leu	Thr	Lys	Leu

465 470 475 480 Thr Glu Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly 485 490 Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys 505 Arg Ser Lys Ile Lys Val Asn Gly Met Val Asn Ile Asp Met Tyr Gly 520 Ile Ile Thr Asp Lys Val Lys Leu Ser Ser Tyr Lys Leu Asn Ala Val Ala Glu Ala Val Leu Lys Asp Lys Lys Lys Asp Leu Ser Tyr Arg Asp Ile Pro Ala Tyr Tyr Ala Ser Gly Pro Ala Gln Arg Gly Val Ile Gly 570 Glu Tyr Cys Val Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys 580 Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile 600 Asn Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys Leu Leu Arg Leu Ala Gly Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln Gly Arg Phe Arg Gly Leu Asp Lys Glu Ala Pro Lys Arg Pro Ala 645 Val Pro Arg Gly Glu Gly Glu Arg Pro Gly Asp Gly Asn Gly Asp Glu Asp Lys Asp Asp Glu Asp Gly Asp Glu Asp Gly Asp Glu Arg Glu 680 Glu Val Ala Arg Glu Thr Gly Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asp Pro Val Val Val 705 710 715 Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu 725 730 Cys Phe Ser Thr Leu Ser Leu Arg Pro Glu Ala Val Ala His Leu Glu 740 Ala Asp Arg Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg 775 780 Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser 785 7.90 795

Pro Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu 825 Leu Pro Cys Leu His Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu 840 Met Leu Leu Ala Thr Arg Ala Tyr Val His Ala Arg Trp Ala Glu Phe 855 Asp Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Gly Met Arg Ala Pro 870 Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe 890 Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Val Ala Met Gly Asp Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys 920 Leu Glu Cys Glu Lys Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys 935 Lys Tyr Ile Gly Val Ile Cys Gly Gly Lys Met Leu Ile Lys Gly Val 950 955 Asp Leu Val Arg Lys Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg 970 Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala 985 Ala Ala Leu Ala Glu Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His 1015 Arg Arg Ile Thr Asp Pro Glu Arg Asp Ile Gln Asp Phe Val Leu 1025 1030 Thr Ala Glu Leu Ser Arg His Pro Arg Ala Tyr Thr Asn Lys Arg 1050 1045 Leu Ala His Leu Thr Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala 1055 1060 Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala 1070 1075 1080 Gln Thr Arg Glu Val Glu Glu Thr Val Ala Arg Leu Ala Ala Leu 1085 1090 1095 Arg Glu Leu Asp Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro 1105 Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser 1120 1125

His Ala Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu 1130 1135 1140

Val Ser Glu Leu Ala Glu Asp Pro Gly Tyr Ala Ile Ala Arg Gly 1145 1150 1155

Val Pro Leu Asn Thr Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala 1160 1165 1170

Ala Cys Val Thr Phe Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile 1175 1180 1185

Thr Glu Ser Leu Leu Lys Arg Phe Ile Pro Glu Thr Trp His Pro 1190 1195 1200

Pro Asp Asp Val Ala Ala Arg Leu Arg Ala Ala Gly Phe Gly Pro  $1205^{\circ}$  1210 1215

Ala Gly Ala Gly Ala Thr Ala Glu Glu Thr Arg Arg Met Leu His 1220 1225 1230

Arg Ala Phe Asp Thr Leu Ala 1235 1240

<210> 16

<211> 1235

<212> PRT

<213> herpes simplex

<400> 16

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 . 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val. Tyr Cys Gly Gly Asp Glu Arg 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg 115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val
130 135 140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr 145 150 155 160

Gly	Met	Arg	Ala	Ala 165	Gln	Phe	His	Ala	Arg 170	Phe	Met	Asp	Ala	Ile 175	Thr
Pro	Thr	Gly	Thr 180	Val	Ile	Thr	Leu	Leu 185	Gly	Leu	Thr	Pro	Glu 190	Gly	His
Arg	Val	Ala 195	Val	His	Val	Tyr	Gly 200	Thr	Arg	Gln	Tyr	Phe 205	Тух	Met	Asn
Lys	Glu 210	Glu	Val	Asp	Arg	His 215	Leu	Gln	Cys	Arg	Ala 220	Pro	Arg	Asp	Leu
Cys 225	Glu	Arg	Met	Ala	Ala 230	Ala	Leu	Arg	Glu	Ser 235	Pro	Gly	Ala	Ser	Phe 240
Arg	Gly	Ile	Ser	Ala 245	Asp	His	Phe	Glu	Ala 250	Glu	Val	Val	Glu	Arg 255	Thr
Asp	Val	Tyr	Tyr 260	Tyr	Glu	Thr	Arg	Pro 265	Ala	Leu	Phe	Tyr	Arg 270	Val	Tyr
Val	Arg	Ser 275	Gly	Arg	Val	Leu	Ser 280	Tyr	Leu	Cys	Asp	Asn 285	Phe	Cys	Pro
Ala	Ile 290	Lys	Lys	Tyr	Glu	Gly 295	Gly	Val	Asp	Ala	Thr 300	Thr	Arg	Phe	Ile
Leu 305	Asp	Asn	Pro	Gly	Phe 310	Val	Thr	Phe	Gly	Trp 315	Tyr	Arg	Leu	Lys	Pro 320
Gly	Arg	Asn	Asn	Thr 325	Leu	Ala	Gln	Pro	Arg 330	Ala	Pro	Met	Ala	Phe 335	Gly
Thr	Ser	Ser	Asp 340	Val	Glu	Phe	Asn	Cys 345	Thr	Ala	Asp	Asn	Leu 350	Ala	Ile
	Gly	355					360					365			
Ile	Glu 370	Cys	Lys	Ala	Gly	Gly 375	Glu	Asp	Glu	Leu	Ala 380	Phe	Pro	Val	Ala
Gly 385	His	Pro	Glu	Asp	Leu 390	Val	Ile	Gln	Ile	Ser 395	Cys	Leu ·	Leu	Tyr	Asp 400
Leu	Ser	Thr	Thr	Ala 405	Leu	Glu	His	Val	Leu 410	Leu	Phe	Ser	Leu	Gly 415	Ser
Cys	Asp	Leu	Pro 420	Glu	Ser	His	Leu	Asn 425	Glu	Leu	Ala	Ala	Arg 430	Gly	Leu
Pro	Thr	Pro 435	Val	Val	Leu	Glu	Phe 440	Asp	Ser	Glu	Phe	Glu 445	Met	Leu	Leu
Ala	Phe 450	Met	Thr	Leu	Val	Lys 455	Gln	Tyr	Gly	Pro	Glu 460	Phe	Val	Thr	Gly
Tyr 465	Asn	Ile	Ile	Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480
Asp	Ile	Tyr	Lys	Val 485	Pro	Leu	Asp	Gly	Tyr 490	Gly	Arg	Met	Asn	Gly 495	Arg

Gly	Val	Phe	Arg 500	Va1	Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg
Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile	Thr 530	Asp	Lys	Ile	Lys	Leu 535	Ser	Ser	Tyr	Ьуs	Leu 540	Asn	Ala	Val	Ala
Glu 545	Ala	Val	Leu	Lys	Asp 550	Lys	Lys	Lys	Asp	Leu 555	Ser	Tyr	Arg	Asp	Ile 560
Pro	Ala	Tyr	Tyr	Ala 565	Ala	${ t Gl}_{m{Y}}$	Pro	Ala	Gln 570	Arg	${ m Gl}_Y$	Val	Ile	Gly 575	Glu
Tyr	Cys	Ile	Gln 580	Asp	Ser	Leu	Leu	Val 585	Gly	Gln	Leu	Phe	Phe 590	Lys	Phe
Leu	Pro	His 595	Leu	Glu	Leu	Ser	Ala 600	Val	Ala	Arg	Leu	Ala 605	Gly	Ile	Asn
Ile	Thr 610	Arg	Thr	Ile	Tyr	Asp 615	Gly	Gln	Gln	Ile	Arg 620	Val	Phe	Thr	Cys
Leu 625	Leu	Arg	Leu	Ala	Asp 630	Gln	Lys	Gly	Phe	Ile 635	Leu	Pro	Asp	Thr	Gln 640
Gly	Arg	Phe	Arg	Gly 645	Ala	Gly	Gly	Glu	Ala 650	Pro	Lys	Arg	Pro	Ala 655	Ala
Ala	Arg	Glu	Asp 660	Glu	Glu	Arg	Pro	Glu 665	Glu	Glu	Gly	Glu	Asp 670	Glu	Asp
Glu	Arg	Glu 675	Glu	Gly	Gly	Gly	Glu 680	Arg	Glu	Pro	Glu	Gly 685	Ala	Arg	Glu
Thr	Ala 690	Gly	Arg	His	Val	Gly 695	Tyr	Gln	Gly	Ala	Arg 700	Val	Leu	Asp	Pro
Thr 705	Ser	Gly	Phe	His	Val 710	Asn	Pro	Val	Val	Val 715	Phe	Asp	Phe	Ala	Ser 720
Leu	Tyr	Pro	Ser	Ile 725	Ile	Gln	Ala	His	Asn 730	Leu	Cys	Phe	Ser	Thr 735	Leu
Ser	Leu	Arg	Ala 740	Asp	Ala	Va1	Ala	His 745	Leu	Glu	Ala	Gly	Lys 750	Asp	Tyr
Leu	Glu	Ile 755	Glu	Val	Gly	Gly	Arg 760	Arg	Leu	Phe	Phe.	Val 765	Lys	Ala	His
Val	Arg 770	Glu	Ser	Leu	Leu	Ser 775	Ile	Leu	Leu	Arg	Asp 780	Trp	Leu	Ala	Met
Arg 785	Lys	Gln	Ile	Arg	Ser 790	Arg	Ile	Pro	Gln	Ser 795	Ser	Pro	Glu	Glu	Ala 800
Val	Leu	Leu	Asp	Lys 805	Gln	Gln	Ala	Ala	Ile 810	Lys	Val	Val	Cys	Asn 815	Ser
Val	Tyr	Gly	Phe	Thr	Gly	Val	Gln	His	Gly	Leu	Leu	Pro	Cys	Leu	His

WO 02/06513

820 825 830

PCT/US01/16525

- Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr  $835 \\ 840 \\ 845$
- Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala 850 855 860
- Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met 865 870 875 880
- Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly 885 890 895
- Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His  $900 \hspace{1.5cm} 905 \hspace{1.5cm} 910$
- Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys 915 920 925
- Thr Phe Thr Lys Leu Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val 930 935 940
- Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys 945 950 955 960
- Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu 965 970 975
- Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu 980 985 990
- Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln 995 1000 1005
- Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp 1010 1015 1020
- Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser 1025 1030 1035
- Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr 1040 1050
- Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile 1055 1060 1065
- Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val 1070 1075 1080
- Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala 1085 1090 1095
- Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser 1100 1105 1110
- Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser His Ala Asp Pro Pro 1115 1120 1125
- Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala 1130 1135 1140

Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr 1145 1150 1155

Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe 1160 1165 1170

Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu 1175 1180 1185

Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala 1190 1195 1200

Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala 1205 1210 1215

Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr 1220 1235 1230

Leu Ala 1235

<210> 17

<211> 1235

<212> PRT

<213> herpes simplex

<400> 17

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 . 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg 115 120 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val 130 135 140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr 145 150 155 160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr 165 170 175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu Cys Glu Arg Met Ala Ala Ala Leu Arg Glu Ser Pro Gly Ala Ser Phe Arg Gly Ile Ser Ala Asp His Phe Glu Ala Glu Val Val Glu Arg Thr Asp Val Tyr Tyr Tyr Glu Thr Arg Pro Ala Leu Phe Tyr Arg Val Tyr Val Arg Ser Gly Arg Val Leu Ser Tyr Leu Cys Asp Asn Phe Cys Pro Ala Ile Lys Lys Tyr Glu Gly Gly Val Asp Ala Thr Thr Arg Phe Ile Leu Asp Asn Pro Gly Phe Val Thr Phe Gly Trp Tyr Arg Leu Lys Pro Gly Arg Asn Asn Thr Leu Ala Gln Pro Arg Ala Pro Met Ala Phe Gly Thr Ser Ser Asp Val Glu Phe Asn Cys Thr Ala Asp Asn Leu Ala Ile Glu Gly Gly Met Ser Asp Leu Pro Ala Tyr Lys Leu Met Cys Phe Asp Ile Glu Cys Lys Ala Gly Gly Glu Asp Glu Leu Ala Phe Pro Val Ala Gly His Pro Glu Asp Leu Val Ile Gln Ile Ser Cys Leu Leu Tyr Asp Leu Ser Thr Thr Ala Leu Glu His Val Leu Leu Phe Ser Leu Gly Ser Cys Asp Leu Pro Glu Ser His Leu Asn Glu Leu Ala Ala Arg Gly Leu Pro Thr Pro Val Val Leu Glu Phe Asp Ser Glu Phe Glu Met Leu Leu Ala Phe Met Thr Leu Val Lys Gln Tyr Gly Pro Glu Phe Val Thr Gly Tyr Asn Ile Ile Asn Phe Asp Trp Pro Phe Leu Leu Ala Lys Leu Thr Asp Ile Tyr Lys Val Pro Leu Asp Gly Tyr Gly Arg Met Asn Gly Arg Gly Val Phe Arg Val Trp Asp Ile Gly Gln Ser His Phe Gln Lys Arg 

Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile	Thr 530	Asp	Lys	Ile	Lys	Leu 535	Ser	Ser	Tyr	Lys	Leu 540	Asn	Ala	Val	Ala
Glu 545	Ala	Val	Leu	Lys	Asp 550	Lys	Lys	Lys	Asp	Leu 555	Ser	Tyr	Arg	Asp	Ile 560
Pro	Ala	Tyr	Tyr	Ala 565	Ala	Gly	Pro	Ala	Gln 570	Arg	Gly	Val	Ile	Gly 575	Glu
Туг	Cys	Ile	Gln 580	Asp	Ser	Leu	Leu	Val 585	Gly	Gln	Leu	Phe	Phe 590	Lys	Phe
Leu	Pro	His 595	Leu	Glu	Leu	Ser	Ala 600	Val	Ala	Arg	Leu	Ala 605	Gly	Ile	Asn
Ile	Thr 610	Arg	Thr	Ile	Tyr	Asp 615	Gly	Gln	Gln	Ile	Arg 620	Val	Phe	Thr	Cys
Leu 625	Leu	Arg	Leu	Ala	Asp 630	Gln	Lys	Gly	Phe	Ile 635	Leu	Pro	Asp	Thr	Gln 640
Gly	Arg	Phe	Arg	Gly 645	Ala	Gly	Gly	Glu	Ala 650	Pro	Lys	Arg	Pro	Ala 655	Ala
Ala	Arg	Glu	Asp 660	Glu	Glu	Arg	Pro	Glu 665	Glu	Glu	Gly	Glu	Asp 670	Glu	Asp
Glu	Arg	Glu 675	Glu	Gly	Gly	Gly	Glu 680	Arg	Glu	Pro	Glu	Gly 685	Ala	Arg	Glu
Thr	Ala 690	Gly	Arg	His	Val	Gly 695	Tyr	Gln	Gly	Ala	Arg 700	Val	Leu	Asp	Pro
Ile 705	Ser	Gly	Phe	His	Val 710	Asn	Pro	Val	Val	Val 715	Phe	Asp	Phe	Ala	Ser 720
Leu	Tyr	Pro	Ser	Ile 725	Ile	Gln	Ala	His	Asn 730	Leu	Cys	Phe	Ser	Thr 735	Leu
Ser	Leu	Arg	Ala 740	Asp	Ala	Val	Ala	His 745	Leu	Glu	Ala	Gly	Lys 750	Asp	Tyr
Leu	Glu	Ile 755	Glu	Val	Gly	Gly	Arg 760	Arg	Leu	Phe	Phe	Val 765	Lys	Ala	His
Val	Arg 770	Glu	Ser	Leu	Leu	Ser 775	Ile	Leu	Leu	Arg	Asp 780	Trp	Leu	Ala	Met
Arg 785	Lys	Gln	Ile	Arg	Ser 790	Arg	Ile	Pro	Gln	Ser 795	Ser	Pro	Glu	Glu	Ala 800
Val	Leu	Leu	Asp	Lys 805	Gln	Gln	Ala	Ala	Ile 810	Lys	Val	Val	Cys	Asn 815	Ser
Val	Tyr	Gly	Phe 820	Thr	Gly	Va1	Gln	His 825	Gly	Leu	Leu	Pro	Cys 830	Leu	His
Val	Ala	Ala 835	Thr	Val	Thr	Thr	Ile 840	Gly	Arg	Glu	Met	Leu 845	Leu	Ala	Thr

Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly Leu Thr Ala Ala Gly Leu Thr Ala Met Gly Asp Lys Met Ala Ser His 900 905 Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys 920 Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val 935 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys 950 955 Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu 985 Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln 1000 Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp 1015 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser 1030 1025 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr 1045 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile 1060 Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val 1075 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser 1105 Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser Pro Ala Asp Pro Pro 1120 1115 Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala 1135 1140 1130 Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr 1150 1155 1145 Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe

1160 1165 1170 Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu 1180 1185 Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Thr 1195 Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala 1205 1210 1215 Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr 1225 1230 Leu Ala 1235 <210> 18 <211> 1235 <212> PRT <213> herpes simplex <400> 18 Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 25 Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 40 Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val 130 135 Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr 1.65 170 Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His 180 Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn

200

Lys	Glu 210	Glu	Val	Asp	Arg	His 215	Leu	Gln	Cys	Arg	Ala 220	Pro	Arg	Asp	Leu
Cys 225	Glu	Arg	Met	Ala	Ala 230	Ala	Leu	Arg	Glu	Ser 235	Pro	Gly	Ala	Ser	Phe 240
Arg	Gly	Ile	Ser	Ala 245	Asp	His	Phe	Glu	Ala 250	Glu	Val	Val	Glu	Arg 255	Thr
Asp	Val	Tyr	Туr 260	Tyr	Glu	Thr	Arg	Pro 265	Ala	Leu	Phe	Tyr	Arg 270	Val	Tyr
Val	Arg	Ser 275	Gly	Arg	Val	Leu	Ser 280	Tyr	Leu	Cys	Asp	Asn 285	Phe	Cys	Pro
Ala	Ile 290	Lys	Lys	Tyr	Glu	Gly 295	Gly	Val	Asp	Ala	Thr 300	Thr	Arg	Phe	Ile
Leu 305	Asp	Asn	Pro	Gly	Phe 310	Val	Thr	Phe	Gly	Trp 315	Tyr	Arg	Leu	Lys	Pro 320
Gly	Arg	Asn	Asn	Thr 325	Leu	Ala	Gln	Pro	Arg 330	Ala	Pro	Met	Ala	Phe 335	Gly
Thr	Ser	Ser	Asp 340	Val	Glu	Phe	Asn	Cys 345	Thr	Ala	Asp	Asn	Leu 350	Ala	Ile
Glu	Gly	Gly 355	Met	Ser	Asp	Leu	Pro 360	Ala	Tyr	Lys	Leu	Met 365	Cys	Phe	Asp
Ile	Glu 370	Cys	Lys	Ala	Gly	Gly 375	Glu	Asp	Glu	Leu	Ala 380	Phe	Pro	Val	Ala
Gly 385	His	Pro	Glu	Asp	Leu 390	Val	Ile	Gln	Ile	Ser 395	Cys	Leu	Leu	Tyr	Asp 400
Leu	Ser	Thr	Thr	Ala 405	Leu	Glu	His	Val	Leu 410	Leu	Phe	Ser	Leu	Gly 415	Ser
Cys	Asp	Leu	Pro 420	Glu	Ser	His	Leu	Asn 425	Glu	Leu	Ala	Ala	Arg 430	Gly	Leu
Pro	Thr	Pro 435	Val	Val	Leu	Glu	Phe 440	Asp	Ser	Glu	Phe	Glu 445	Met	Leu	Leu
Ala	Phe 450	Met	Thr	Leu	Val	Lys 455	Gln	Tyr	Gly	Pro	Glu 460	Phe	Val	Thr	Gly
Tyr 465	Asn	Ile	Ile	Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480
Asp	Ile	Tyr	Lys	Val 485	Pro	Leu	Asp	Gly	Туг 490	Gly	Arg	Met	Asn	Gly 495	Arg
Gly	Val	Phe	Arg 500	Val	Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg
Ser	Lys	Ile 515	Lys	Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile	Thr	Asp	Lys	Ile	Lys	Leu	Ser	Ser	Tyr	Lys	Leu	Asn	Ala	Val	Ala

530 535 540

Glu Ala Val Leu Lys Asp Lys Lys Asp Leu Ser Tyr Arg Asp Ile Pro Thr Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu 570 Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe 585 Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn 600 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Gln Ile Arg Val Phe Thr Cys Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln 635 Gly Arg Phe Arg Gly Ala Gly Glu Ala Pro Lys Arg Pro Ala Ala Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asn 665 Glu Arg Glu Gly Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro 695 Thr Ser Gly Phe His Val Asn Pro Val Val Phe Asp Phe Ala Ser 710 715 Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu 730 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser 805 810 Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His 825 Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr 840 Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala

. 855

59

Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met 870 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly 890 885 Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His Ile Ser Arg Ala Leu Phe Leu Pro Pro Ile Lys Leu Glu Cys Glu Lys 920 Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val 935 Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys 950 955 Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu 970 Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Leu Ala Glu 985 Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp 1015 Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser 1025 1030 Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr 1045 Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val 1075 Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala 1085 1090 Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser Pro Ala Lys Arg Pro Arg Glu Thr Pro Ser Pro Ala Asp Pro Pro Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala 1135 Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr 1150 Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe 1165 1170 Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu 1175 1180 1185

Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala 1190 1195 1200

Ala Arg Leu Arg Thr Ala Gly Phe Gly Ala Val Gly Ala Gly Ala 1205 1210 1215

Thr Ala Glu Glu Thr Arg Arg Met Leu His Arg Ala Phe Asp Thr 1220 1225 1230

Leu Ala 1235

<210> 19

<211> 1235

<212> PRT

<213> herpes simplex

<400> 19

Met Phe Ser Gly Gly Gly Pro Leu Ser Pro Gly Gly Lys Ser Ala 1 5 10 15

Ala Arg Ala Ala Ser Gly Phe Phe Ala Pro Ala Gly Pro Arg Gly Ala 20 25 30

Gly Arg Gly Pro Pro Pro Cys Leu Arg Gln Asn Phe Tyr Asn Pro Tyr 35 40 45

Leu Ala Pro Val Gly Thr Gln Gln Lys Pro Thr Gly Pro Thr Gln Arg 50 55 60

His Thr Tyr Tyr Ser Glu Cys Asp Glu Phe Arg Phe Ile Ala Pro Arg 65 70 75 80

Val Leu Asp Glu Asp Ala Pro Pro Glu Lys Arg Ala Gly Val His Asp 85 90 95

Gly His Leu Lys Arg Ala Pro Lys Val Tyr Cys Gly Gly Asp Glu Arg 100 105 110

Asp Val Leu Arg Val Gly Ser Gly Gly Phe Trp Pro Arg Arg Ser Arg 115 120 . 125

Leu Trp Gly Gly Val Asp His Ala Pro Ala Gly Phe Asn Pro Thr Val 130 135 140

Thr Val Phe His Val Tyr Asp Ile Leu Glu Asn Val Glu His Ala Tyr 145 150 155 160

Gly Met Arg Ala Ala Gln Phe His Ala Arg Phe Met Asp Ala Ile Thr 165 170 175

Pro Thr Gly Thr Val Ile Thr Leu Leu Gly Leu Thr Pro Glu Gly His

Arg Val Ala Val His Val Tyr Gly Thr Arg Gln Tyr Phe Tyr Met Asn 195 200 205

Lys Glu Glu Val Asp Arg His Leu Gln Cys Arg Ala Pro Arg Asp Leu 210 215 220

Cys Glu 225	Arg Me	t Ala	Ala 230	Ala	Leu	Arg	Glu	Ser 235	Pro	Gly	Ala	Ser	Phe 240
Arg Gly	Ile Se	r Ala 245	Asp	His	Phe	Glu	Ala 250	Glu	Val	Val	Glu	Arg 255	Thr
Asp Val	Tyr Ty 26	_	Glu	Thr	Arg	Pro 265	Ala	Leu	Phe	Tyr	Arg 270	Val	Tyr
Val Arg	Ser Gl 275	y Arg	Val	Leu	Ser 280	Tyr	Leu	Cys	Asp	Asn 285	Phe	Cys	Pro
Ala Ile 290	Lys Ly	s Tyr	Glu	Gly 295	Gly	Val	Asp	Ala	Thr 300	Thr	Arg	Phe	Ile
Leu Asp 305	Asn Pr	o Gly	Phe 310	Val	Thr	Phe	Gly	Trp 315	Tyr	Arg	Leu	Lys	Pro 320
Gly Arg	Asn As	n Thr 325	Leu	Ala	Gln	Pro	Arg 330	Ala	Pro	Met	Ala	Phe 335	Gly
Thr Ser	Ser As	-	Glu	Phe	Asn	Cys 345	Thr	Ala	Asp	Asn	Leu 350	Ala	Ile
Glu Gly	Gly Me 355	t Ser	Asp	Leu	Pro 360	Ala	Tyr	Lys	Leu	Met 365	Cys	Phe	Asp
Ile Glu 370	Суѕ Ту	s Ala	Gly	Gly 375	Glu	Asp	Glu	Leu	Ala 380	Phe	Pro	Val	Ala
Gly His 385	Pro Gl	u Asp	Leu 390	Val	Ile	Gln	Ile	Ser 395	Cys	Leu	Leu	Tyr	Asp 400
Leu Ser	Thr Th	r Ala 405	Leu	Glu	His	Val	Leu 410	Leu	Phe	Ser	Leu	Gly 415	Ser
Cys Asp	Leu Pr 42		Ser	His	Leu	Asn 425	Glu	Leu	Ala	Ala	Arg 430	Gly	Leu
Pro Thr	Pro Va 435	l Val	Leu	Glu	Phe 440	Asp	Ser	Glu	Phe	Glu 445	Met	Leu	Leu
Ala Phe 450	Met Th	ır Leu	Val	Lys 455	Gln	Tyr	Gly	Pro	Glu 460	Phe	Val	Thr	Gly
Tyr Asn 465	Ile Il	e Asn	Phe 470	Asp	Trp	Pro	Phe	Leu 475	Leu	Ala	Lys	Leu	Thr 480
Asp Ile	Tyr Ly	rs Val 485	Pro	Leu	Asp	Gly	Туг 490	Gly	Arg	Met	Asn	Gly 495	Arg
Gly Val	Phe Ar 50		Trp	Asp	Ile	Gly 505	Gln	Ser	His	Phe	Gln 510	Lys	Arg
Ser Lys	Ile Ly 515	s Val	Asn	Gly	Met 520	Val	Asn	Ile	Asp	Met 525	Tyr	Gly	Ile
Ile Thr 530	Asp Ly	s Ile	Lys	Leu 535	Ser	Ser	Tyr	Lys	Leu 540	Asn	Ala	Val	Ala
Glu Ala 545	Val L∈	u Lys	Asp 550	Lys	Lys	Lys	Asp	Leu 555	Ser	Tyr	Arg	Asp	Ile 560

Pro Ala Tyr Tyr Ala Ala Gly Pro Ala Gln Arg Gly Val Ile Gly Glu Tyr Cys Ile Gln Asp Ser Leu Leu Val Gly Gln Leu Phe Phe Lys Phe Leu Pro His Leu Glu Leu Ser Ala Val Ala Arg Leu Ala Gly Ile Asn 600 Ile Thr Arg Thr Ile Tyr Asp Gly Gln Ile Arg Val Phe Thr Cys 615 Leu Leu Arg Leu Ala Asp Gln Lys Gly Phe Ile Leu Pro Asp Thr Gln 630 635 Gly Arg Phe Arg Gly Gly Gly Glu Ala Pro Lys Arg Pro Ala Ala 650 Ala Arg Glu Asp Glu Glu Arg Pro Glu Glu Glu Gly Glu Asp Glu Asp Glu Arg Glu Glu Gly Gly Glu Arg Glu Pro Glu Gly Ala Arg Glu Thr Ala Gly Arg His Val Gly Tyr Gln Gly Ala Arg Val Leu Asp Pro Thr Ser Gly Phe His Val Asn Pro Val Val Phe Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Gln Ala His Asn Leu Cys Phe Ser Thr Leu 730 Ser Leu Arg Ala Asp Ala Val Ala His Leu Glu Ala Gly Lys Asp Tyr Leu Glu Ile Glu Val Gly Gly Arg Arg Leu Phe Phe Val Lys Ala His 760 Val Arg Glu Ser Leu Leu Ser Ile Leu Leu Arg Asp Trp Leu Ala Met Arg Lys Gln Ile Arg Ser Arg Ile Pro Gln Ser Ser Pro Glu Glu Ala 790 795 Val Leu Leu Asp Lys Gln Gln Ala Ala Ile Lys Val Val Cys Asn Ser Val Tyr Gly Phe Thr Gly Val Gln His Gly Leu Leu Pro Cys Leu His 825 Val Ala Ala Thr Val Thr Thr Ile Gly Arg Glu Met Leu Leu Ala Thr Arg Glu Tyr Val His Ala Arg Trp Ala Ala Phe Glu Gln Leu Leu Ala 855 Asp Phe Pro Glu Ala Ala Asp Met Arg Ala Pro Gly Pro Tyr Ser Met 875 Arg Ile Ile Tyr Gly Asp Thr Asp Ser Ile Phe Val Leu Cys Arg Gly

885 890 895

- Leu Thr Ala Ala Gly Leu Thr Ala Val Gly Asp Lys Met Ala Ser His
  900 905 910
- Ile Ser Arg Ala Leu Phe Leu Ser Pro Ile Lys Leu Glu Cys Glu Lys 915 920 925
- Thr Phe Thr Lys Leu Leu Ile Ala Lys Lys Lys Tyr Ile Gly Val 930 935 940
- Ile Tyr Gly Gly Lys Met Leu Ile Lys Gly Val Asp Leu Val Arg Lys 945 950 955 960
- Asn Asn Cys Ala Phe Ile Asn Arg Thr Ser Arg Ala Leu Val Asp Leu 965 970 975
- Leu Phe Tyr Asp Asp Thr Val Ser Gly Ala Ala Ala Ala Leu Ala Glu 980 985 990
- Arg Pro Ala Glu Glu Trp Leu Ala Arg Pro Leu Pro Glu Gly Leu Gln 995 1000 1005
- Ala Phe Gly Ala Val Leu Val Asp Ala His Arg Arg Ile Thr Asp 1010 1015 1020
- Pro Glu Arg Asp Ile Gln Asp Phe Val Leu Thr Ala Glu Leu Ser 1025 1030 1035
- Arg His Pro Arg Ala Tyr Thr Asn Lys Arg Leu Ala His Leu Thr 1040 1050
- Val Tyr Tyr Lys Leu Met Ala Arg Arg Ala Gln Val Pro Ser Ile 1055 1060 1065
- Lys Asp Arg Ile Pro Tyr Val Ile Val Ala Gln Thr Arg Glu Val 1070 1075 1080
- Glu Glu Thr Val Ala Arg Leu Ala Ala Leu Arg Glu Leu Asp Ala 1085 1090 1095
- Ala Ala Pro Gly Asp Glu Pro Ala Pro Pro Ala Ala Leu Pro Ser 1100 1105 1110
- Pro Ala Lys Arg Pro Arg Glu Thr Pro Leu His Ala Asp Pro Pro 1115 1120 1125
- Gly Gly Ala Ser Lys Pro Arg Lys Leu Leu Val Ser Glu Leu Ala 1130 1135 1140
- Glu Asp Pro Ala Tyr Ala Ile Ala His Gly Val Ala Leu Asn Thr 1145 1150 1155
- Asp Tyr Tyr Phe Ser His Leu Leu Gly Ala Ala Cys Val Thr Phe 1160 1165 1170
- Lys Ala Leu Phe Gly Asn Asn Ala Lys Ile Thr Glu Ser Leu Leu 1175 1180 1185
- Lys Arg Phe Ile Pro Glu Val Trp His Pro Pro Asp Asp Val Ala 1190 1195 1200

Ala Arg Leu Arg Ala Ala Gly Phe Gly Ala Val Gly Ala Gly Ala 1205 1210 1215

Leu Ala 1235

## (19) World Intellectual Property Organization International Bureau





(43) International Publication Date 24 January 2002 (24.01.2002)

**PCT** 

# (10) International Publication Number WO 02/006513 A3

- (51) International Patent Classification<sup>7</sup>: G01N 33/569, A61P 31/22, C07K 14/00
- (21) International Application Number: PCT/US01/16525
- (22) International Filing Date: 13 July 2001 (13.07.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:

60/218,118 13 July 2000 (13.07.2000) US 60/283,880 13 April 2001 (13.04.2001) US

- (71) Applicant (for all designated States except US): PHAR-MACIA & UPJOHN COMPANY [US/US]; 301 Henrietta Street, Kalamazoo, MI 49001 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): HOMA, Fred, L. [US/US]; 3430 Pine Grove Lane, Kalamazoo, MI 49008 (US). WATHEN, Michael, W. [US/US]; 6474 Pepperidge, Portage, MI 49002 (US). HOPKINS, Todd, A. [US/US]; 744 Sarah Street, Galesburg, MI 49053 (US). THOMSEN, Darrel, R. [US/US]; 6916 Willson Drive, Kalamazoo, MI 49009 (US).

- (74) Agent: YANG, Lucy, X.; Intellectual Property Legal Services, Pharmacia & Upjohn Company, 301 Henrietta Street, Kalamazoo, MI 49001 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- (88) Date of publication of the international search report: 23 January 2003

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



02/006513 A3

(54) Title: A METHOD FOR TREATING HERPES VIRUSES

(57) Abstract: The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpesvrus in a human host in need of such treatment. The present invention relates to a method for selecting an anti-herpes viral compound and a method for selectively inhibiting herpsvrus in a human host in need of such treatment.

Inter nal Application No PCT/US 01/16525

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 G01N33/569 A61F C07K14/00 A61P31/22 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 GO1N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. EP 0 097 633 A (SUNDQVIST VIVI ANNE 1,2,4,5, ;WAHREN BRITTA (SE); HARMENBERG JOHAN 8,9,11, (SE)) 4 January 1984 (1984-01-04) 12,16, 17,20, 23-26 the whole document WO 98 04707 A (MCLEAN GORDON WILLIAM Α 1,2,4,5, ; MEDICAL RES COUNCIL (GB); STOW NIGEL 8,9,11, DENNIS) 5 February 1998 (1998-02-05) 12, 16, 17,20. 23-26 abstract -/--Further documents are listed in the continuation of box C. Χ Patent family members are listed in annex. Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled other means document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 30 September 2002 07/10/2002 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31~70) 340-2040, Tx. 31 651 epo nl, Fax: (+31~70) 340-3016 Moreno, C

Inter nal Application No
PCT/US 01/16525

		PC1/U3 01/10525
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 00 40563 A (STROHBACH JOSEPH WALTER;SCOTT ALLEN (US); UPJOHN CO (US); SCHNUTE) 13 July 2000 (2000-07-13)	1,2,4,5, 8,9,11, 12,16, 17,20, 23-26
	abstract 	
P,A	WO 00 40561 A (STROHBACH JOSEPH WALTER;UPJOHN CO (US); SCHNUTE MARK E (US); THAI) 13 July 2000 (2000-07-13)	1,2,4,5, 8,9,11, 12,16, 17,20, 23-26
	abstract	25 25
Α	WO 94 24296 A (UNIV SASKATCHEWAN) 27 October 1994 (1994-10-27) abstract	25,26
		•
	<u></u>	

national application No. PCT/US 01/16525

Box I Observations where certain claims were found unsearchable (Continuation	of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 1	7(2)(a) for the following reasons:
Claims Nos.:     because they relate to subject matter not required to be searched by this Authority, namely:	
Claims Nos.:  because they relate to parts of the International Application that do not comply with the pres an extent that no meaningful International Search can be carried out, specifically:  see FURTHER INFORMATION sheet PCT/ISA/210	cribed requirements to such
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and	third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of 1	irst sheet)
This International Searching Authority found multiple inventions in this international application, as follows:	lows:
As all required additional search fees were timely paid by the applicant, this International Se searchable claims.	earch Report covers all
2. As all searchable claims could be searched without effort justifying an additional fee, this Au of any additional fee.	nthority did not invite payment
3. As only some of the required additional search fees were timely paid by the applicant, this licenses only those claims for which fees were paid, specifically claims Nos.:	nternational Search Report
4. No required additional search fees were timely paid by the applicant. Consequently, this Interestricted to the invention first mentioned in the claims; it is covered by claims Nos.:	ernational Search Report is
Remark on Protest  The additional search fees were accommodified the payment of t	

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

#### Continuation of Box I.2

Present claims 23 and 24 relate to a compound defined by reference to a desirable characteristic or property, namely the change of the wild type HSV-1 polymerases at amino acid 823 from valine to alanine in the presence of said compound.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds 1–17 in figure 1.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

Tuiormation on patent family members

Interional Application No
PCT/US 01/16525

Patent document cited in search report		Publication date		Patent family member(s)	Publication date		
EP 0097633	Α	04-01-1984	DE	3363728 D1	03-07-1986		
			EP	0097633 A1	04-01-1984		
			SE	8203909 A	24-12-1983		
WO 9804707	Α	05-02-1998	AU	3701397 A	20-02-1998		
			EP	0918866 A1	02-06-1999		
			WO	9804707 A1	05-02-1998		
			US	6337074 B1	08-01-2002		
WO 0040563	Α	13-07-2000	AU	2158300 A	24-07-2000		
			BR	9916781 A	04-12-2001		
			CN	1332729 T	23-01-2002		
			CZ	20012458 A3	12-12-2001		
			EΡ	1140851 A1	10-10-2001		
			NO	20013379 A	06-07-2001		
			PL	348769 A1	17-06-2002		
			SK	8312001 A3	03-12-2001		
			TR	200101893 T2	21-11-2001		
			WO	0040563 A1	13-07-2000		
			US 	6248736 B1	19-06-2001 		
WO 0040561	Α	13-07-2000	AU	2348600 A	24-07-2000		
			CN	1333753 T	30-01-2002		
			CZ	20012454 A3	13-03-2002		
			EP	1140850 A1	10-10-2001		
			NO	20013383 A	07-09-2001		
			TR	200101906 T2	21-12-2001		
			WO	0040561 A1	13-07-2000		
			US 	6248739 B1	19-06-2001 		
WO 9424296	Α	27-10-1994	WO	9424296 A2	27-10-1994		
			US	6086902 A	11-07-2000		